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VERTIGO.[1]

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THE occurrence of vertigo or dizziness is not an uncommon symptom, and it is one which causes great distress to the patient and, if it is not speedily relieved, to his attendant physician also.

Vertigo may be defined as an hallucination of movement, and is synonymous with dizziness or giddiness. It is necessary to ascertain tactfully that the patient is not labelling vague sensations such as "clouding before the eyes" and "faintness" as giddiness because he cannot find a more suitable description. In true vertigo there is always a disturbance of some part of the vestibular system, either central or peripheral, even though the precipitating cause may be far removed. An example of this is the vertigo of circulatory failure. Associated with the vertigo there is a loss of confidence which may, in some cases, be so pronounced that the organic basis of the patient's symptoms is not fully appreciated.

Man is not generally conscious of the action of his labyrinths in balancing. However, these specialized sense organs are constantly functioning and he becomes aware of their existence only when something goes wrong.

The intensity of the symptoms depends largely on the rate at which the causative lesion develops. If it is rapid, the vertigo is intense; if it is gradual, the symptoms are milder. When the symptoms are acute, nausea and vomiting occur, and this is due to the overflow of impulses from the vestibular nuclei to the adjacent vagal nuclei.

Owing to the close association of the labyrinth and cochlea, disturbances of the latter are frequent in end organ lesions, and varying degrees of deafness and tinnitus may occur.

It is important to decide whether the cause of the vertigo is in the central or peripheral vestibular system, and this necessitates a detailed examination by the otologist, as well as examination of the central nervous and cardio-vascular systems.

In this paper we shall consider only peripheral causes, and the others will be discussed by another speaker.

Classification of vertigo of peripheral origin is difficult, and the fact that every authority has a different one suggests that none is really satisfactory. The following compromise is, from the practical viewpoint, as good as any.

AURAL VERTIGO.

Aural vertigo may be classified under the following headings: (i) Vertigo with associated cochlear symptoms

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on May 28, 1953.

(Ménière's syndrome): (*a*) acute, (*b*) subacute and chronic. (ii) Aural vertigo without cochlear symptoms: (*a*) vestibular neurinitis, (*b*) positional vertigo, (*c*) motion sickness.

In peripheral lesions vertigo is usually of sudden onset, is tactile (definite sensation of movement) or turning, is not followed by loss of consciousness and is rarely preceded by headache. If nystagmus is present, the movements are of the same intensity and frequency and are horizontal or rotational in type and never vertical. Falling is towards the slow component, the direction of falling is altered by change in position of the head, and past pointing occurs. Spontaneous nystagmus, due to a lesion of the end organ, rarely lasts for more than three weeks and is always accompanied by the sensation of vertigo. With central lesions nystagmus may be present for prolonged periods and can be of any type, including vertical, and falling is often in the direction of the fast component and is little influenced by position of the head. Vertigo with loss of consciousness or localized severe headache is usually indicative of a central lesion.

A routine examination of the ear, nose and throat should be followed by the following tests.

1. Estimation of hearing. Hearing estimation should be made by the whispered and conversational voice test, masking being used, particularly if there is much difference in the hearing in the two ears, and routine tuning fork tests.

2. A full audiogram of both air and bone conduction. In obscure cases a loudness balance test should be made as well. This is a test for the so-called recruitment phenomenon. When recruitment is present, although hearing is subnormal for sounds at low sensation level, it is more nearly normal for sounds of higher sensation level and is due to the existence of the "all or none" reaction of conductivity in nerve tissue. Recruitment is present only in perceptive deafness due to an end organ lesion, and does not occur with a lesion of the auditory nerve or middle ear. It is the presence of recruitment which makes perceptive deaf people intolerant of noise of high intensity.

3. Tests of vestibular function. The most effective and practical test is the modification of the alternate hot and cold caloric tests as devised by Cawthorne, Fitzgerald and Hallpike. For this test the patient reclines with the head raised 30° from the horizontal and the eyes fixed in the mid-position on a spot on the ceiling. Water at 30° C. is used for the cold test and at 44° C. for the hot test, and at least five minutes should be left between tests. Each ear is irrigated for forty seconds at a constant flow with a cannula of four millimetres bore, and the vessel containing the water is placed two feet above the head. The resulting nystagmus is timed accurately, the time being taken conventionally as from the commencement of the stimulus to the end point of the nystagmus. The normal response is from one and a quarter to two and a half minutes. By the use of both the hot and cold tests, small variations from the normal become more apparent, and as the stimulation is minimal the test should cause no undue discomfort to the patient. Should either or both ears fail to react, water at 20° C. may be used to see if any reaction can be elicited.

These tests will give the following results: (i) Normal: with approximately equal response from each ear to both the hot and cold test. (ii) Abnormal: (*a*) hypoactive—decreased response for both hot and cold from one or both sides (canal paresis); (*b*) directional preponderance—there is a readiness of nystagmus to occur to one side more than the other (utricular paresis); (*c*) combination of both the foregoing.

Where some middle ear condition contraindicates caloric testing, cold air may be used or the rotational testing with a Barany's chair, or the culpometric tests of Egmond or the galvanic test. These tests require special equipment and are not generally practicable.

Test for Positional Nystagmus.

Nystagmus is looked for after rapid head movement from the vertical to the horizontal with the head turned first to one side and then to the other. In some cases nystagmus appears after a few seconds and lasts only ten to twenty seconds and cannot be reelicited for half an hour or more afterwards even if the same position is adopted. This indicates a lesion in the vestibular labyrinth, whereas positional nystagmus without much dizziness, which is not fatigable, is usually due to a central lesion.

Causes of Aural Vertigo.

The causes of aural vertigo may be summarized as follows.

1. Acute aural vertigo may be due to any of the following disorders: (*a*) in the external ear, *otitis externa* or occlusive wax; (*b*) in the middle ear, Eustachian tube obstruction, otitic barotrauma or *otitis media*; (*c*) in the inner ear, a vascular catastrophe, a fracture of the temporal bone involving the otic capsule, labyrinthitis secondary to tympanic or meningitic infection, Ménière's disease, toxic labyrinthitis, or epidemic labyrinthitis (perhaps of virus origin). Apart from the epidemic type of toxic labyrinthitis mentioned, tobacco, alcohol, salicylates and quinine are the most common toxic agents. However, arsenic, lead, phosphorus, carbon monoxide, carbon disulphide, oil of chenopodium, mercury and aniline dye (used in hair dyes) are all proven toxic agents.

2. Subacute or chronic aural vertigo may have as its cause any of the following disorders: (*a*) in the middle ear, chronic Eustachian tube obstruction or chronic *otitis media*, especially with a fistula; (*b*) in the inner ear, otosclerosis, toxic labyrinthitis, Ménière's disease, degenerative changes due to vascular or idiopathic causes, or eighth nerve tumour.

3. Aural vertigo without cochlear symptoms may be due to: (*a*) vestibular neurinitis—this is a toxic effect as exemplified by streptomycin; (*b*) positional vertigo, when there is a localized lesion of the labyrinth, either from trauma or some toxic effect; (*c*) motion sickness, caused by excessive stimulation of the semicircular canals.

Treatment.

The most dramatic relief follows appropriate treatment of the simpler abnormal otitic conditions. In all acute cases complete rest in bed with little head movement is desirable and sedation with barbiturates is helpful. "Avomine" or "Andramine" frequently appears to give relief, especially in the acute phase. When the labyrinth has been destroyed as the result of an acute inner ear condition, complete relief of symptoms occurs within a few weeks. However, if the labyrinth is severely damaged but still functioning slightly, mild symptoms may persist for a long period.

Hydrops of the Labyrinth or Ménière's Disease.

Ménière's disease is a more common condition than is generally supposed, affecting mainly the forty to sixty years age group. The pathology of Ménière's disease is well known since Hallpike and Cairns's description of the endolymphatic distension, but the actual ætiology is obscure. The disease is usually limited to one labyrinth, although in 20% of cases both are eventually affected. There is a sudden temporary variation of labyrinthine output, which wears off in time. However, there is usually some permanent impairment of the labyrinthine function, and periodic attacks with remissions are the rule. After one severe or several mild attacks there is usually some perceptive deafness and generally some abnormality in the caloric responses. Once the diagnosis has been firmly established, the patient should have the condition explained to him so that he appreciates the underlying cause, and must be reassured about "tumours on the brain" and other fears which, owing to the distressing symptoms, he naturally has. Apart from the acoustic neurofibroma, it is unusual, though not impossible, for deafness to be associated with vertigo due to a central cause.

Treatment is by mild sedation, a salt-free diet and the administration of ammonium chloride (15 grains three times a day), and restriction of fluid intake to not more than two and a half pints in twenty-four hours. This régime prevents unnecessary fluid retention and is helpful in a large proportion of cases.

Histamine injections help in some cases (intravenous injections of two milligrammes of histamine in 250 cubic centimetres of normal saline on three successive days, later one milligramme injected subcutaneously per week). Probably better is the administration of 100 milligrammes of nicotinic acid three times a day. This is easier to administer, particularly over a period of time, and statistically gives better results than any other form of conservative treatment. Both these treatments are based on the vasomotor theory of the causation of the hydrops.

In severe cases of bilateral hydrops, in which the previous methods fail, cessation of vestibular function may be brought about by giving streptomycin. This is a recent form of treatment and is not recommended for general use, but is probably valuable in selected cases. Streptomycin is given daily until caloric reaction of the labyrinth is abolished, and the hearing is checked frequently by the audiometer.

Surgical Treatment.

In severe cases, in which there are unilateral signs and no useful hearing is present, destruction of the labyrinth by labyrinthectomy is indicated, by the method used and described by Cawthorne. This is a simple operation, the patient being out of hospital in two weeks and usually able to return to work within two months of operation. It is, of course, out of the question when there is any useful degree of hearing present, or if there is any suggestion of involvement of the other ear. In properly selected cases this gives excellent results.

Intracranial Section of the Eighth Nerve.—In operation on the eighth nerve section of the vestibular portion only of the nerve is attempted and the hearing is retained. However, should the condition be severe enough to require operation, useful hearing is rarely present, and the operation is a very much more serious procedure than the aforementioned.

Operations on the Stellate Ganglion.—Operations on the stellate ganglion and the sympathetic plexus around the vertebral artery are stated to prevent the attacks and to reduce or abolish tinnitus without affecting the hearing. This form of treatment is still in the experimental stage. Injection of the stellate ganglion may be tried, and if temporary relief is obtained the complete operation may be performed at a later date.

Vestibular Neuronitis.

Vestibular neuronitis is a toxic condition of the vestibular neurons and tends to affect younger patients than Ménière's disease, being most common in the twenty to thirty years age group. Cochlear symptoms are slight or absent, and the onset frequently follows an infective illness. These patients benefit greatly by removal of any oro-nasal infective foci.

Paroxysmal Positional Vertigo.

Paroxysmal positional vertigo frequently follows an injury to the head, and is probably due to a circumscribed traumatic lesion in the labyrinth which may be likened to a mute note in an otherwise normal piano keyboard. Avoidance of the precipitating head movement should be encouraged, and the ultimate prognosis is good. Recent trials with "Mosidal' (Abbott) have not been very encouraging. Positional nystagmus of the vestibular type occurs when the head is held in a certain position; this must not be confused with the positional nystagmus, often without much dizziness, which occurs with the head in any backwards position and readily reappears when the same position is assumed. This is frequently indicative of a cerebellar lesion.

Eighth Nerve Tumour.

Vertigo is not a prominent symptom of eighth nerve tumour, owing to the slow development of vestibular hypofunction. Classically unilateral nerve deafness is present for a long period before the development of vestibular hypofunction, and lastly symptoms due to involvement of the fifth or seventh nerve appear—the diminished corneal reflex on the side of the lesion being usually the earliest sign. By this time there are usually severe perceptive deafness and absence of caloric responses; these, together with the raised cerebro-spinal fluid protein content and X-ray findings, render the diagnosis certain.

However, many cases are atypical. If there is only partial deafness, a loudness balance test will discriminate between an end organ lesion and a nerve lesion. In a few reported cases in which the deafness has been more of a conductive type, the coexistence of otosclerosis has been suggested. When there is any suggestion of this condition the case should be reviewed from time to time in cooperation with a neurosurgeon.

In the vast majority of cases the otologist can, on clinical, audiometric and vestibular investigation, differentiate accurately between an eighth nerve lesion and an end organ lesion.

Conclusion.

In conclusion, if after a general examination of the nervous and cardio-vascular systems no cause can be found for the vertigo, careful examination of the ear will in most cases permit a diagnosis to be made. Even when treatment is only partially effective, great relief may be given to the patient if he can be given a definite reason why he is having his distressing symptoms. When there is doubt, reexamination and reassessment after a period of some months are required.

VERTIGO.

By C. B. HUDSON,
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THE subject of vertigo is a difficult and important one. It is difficult because the term itself is ill defined and because it is often a symptom of obscure disease processes. It is important because it may be a symptom of a trivial disorder or, on the other hand, it may be a manifestation of serious disease.

There is much difference of opinion as to how the term vertigo should be defined. Russell Brain defines the term as the consciousness of disordered orientation of the body in space; however, he states that the derivation of the term implies a sense of rotation of the patient or of his surroundings, but that this, though frequently present, is not the only form of vertigo as just defined. Others attempt to confine the term to the symptom of a sense of rotation of the patient or of his surroundings and exclude the sense of dizziness often complained of by patients suffering from psychoneurotic disorders. Vertigo usually refers to sudden onset of disordered orientation in space and does not refer to ataxia, which is more gradual in onset and does not produce the same feeling of discomfort as does vertigo.

Before we pass to the consideration of the various causes of vertigo, a short discussion of the mechanisms by which the spatial orientation of the body is maintained seems appropriate.

Balance is maintained by the integration of labyrinthine, visual and kinæsthetic impulses, the last-mentioned originating in the muscles concerned with maintaining the upright posture, but especially in the muscles of the neck. The peripheral vestibular apparatus (semicircular canals, utricle and saccula) is connected with the vestibular nuclei in the medulla by the vestibular nerve. The vestibular nuclei have extensive connexions throughout the central nervous system. They send many fibres to the cerebellum and receive fibres from this organ. The vestibulo-spinal trace is able to influence somatic muscles directly, while fibres passing up in the median longitudinal bundle are connected with the nuclei of the nerves concerned with ocular movements.

Lesions involving any of these connexions may produce vertigo, as may lesions of any of the nervous pathways

concerned with ocular movement. Lesions of the cervical cord, where the reflex centres for tonic neck impulses are situated, seldom result in vertigo.

It should be noted that the vestibular nuclei are situated close to the nucleus of the vagus nerve (*nucleus ambiguus*), so that stimuli reaching the vestibular nuclei may overflow to the nucleus of the vagus. This explains the nausea, vomiting, pallor and loss of consciousness that may accompany severe vertigo.

The determination of the cause of vertigo in a given case would be much less difficult if it was posible, by clinical examination, to ascertain the site of the lesion. In many cases this is impossible, because vertigo is often associated with conditions which are associated with general disturbance of cerebral function. However, a classification of the causes of vertigo according to the site of the lesion forms a satisfactory basis for the differential diagnosis of this symptom.

Vertigo may be divided into the following types:

1. Central vertigo, or vertigo associated with disturbances or disease of the central nervous system.

2. Vertigo due to lesions of the vestibular nerve.

3. Peripheral vertigo, or vertigo associated with disease of the labyrinth.

Central vertigo falls into the sphere of the neurologist, while peripheral vertigo belongs to the sphere of the oto-rhinologist. Vestibular nerve lesions occupy an intermediate position, because such lesions produce both labyrinthine and central effects. Furthermore, certain toxins produce vertigo, yet their site of action has not yet been definitely determined.

When confronted with a patient complaining of vertigo, the diagnostic problem is clarified if it is possible to establish whether the vertigo is peripheral or central in origin. The following points are helpful, but not reliable, guides in this direction.

Peripheral vertigo usually occurs in attacks; it is initiated by motion; it is self-limited; the direction of falling is influenced by the position of the head; tinnitus and deafness are often present; aural abnormalities are often apparent; neurological abnormalities are absent. In the central type the findings are often directly opposite to those cited, and, in addition, spontaneous vertical nystagmus is pathognomonic of a central lesion. If stimulation of one labyrinth produces conjugate deviation of the eyes instead of nystagmus, this is also pathognomonic of a central lesion.

Central Vertigo.

Psychogenic Vertigo.

Psychogenic disorder is often associated with a sense of giddiness or dizziness, but does not cause a sense of violent rotation such as occurs with severe central or peripheral vertigo. The differential diagnosis is made difficult by the fact that organic disease may produce minor forms of vertigo and by the fact that the symptoms of true vertigo are very unpleasant and may themselves produce psychological disorder. A thorough examination of the central nervous system and of the ears, together with psychiatric examination, will usually establish the diagnosis.

Vertigo due to Cortical Disturbance.

Cortical disturbance, such as occurs in epilepsy and migraine, may be accompanied by vertigo. If this symptom occurs as an aura and is followed by typical epileptiform phenomena or by the classical pattern of migraine, the diagnosis is not difficult. If the vertigo occurs as an aura or after-effect of atypical manifestations of these two disorders, it may not be possible to establish a diagnosis without prolonged observation.

Vertigo Associated with General Disturbance of Cerebral Function.

Disturbance of the cerebral circulation or oxygenation or of the intracranial tension may produce vertigo. Anæmia is often associated with minor forms of vertigo, but this is not a striking symptom, unless there is disturbance of the labyrinth, such as sometimes occurs in leuchæmia. Many patients with hypertension or cerebral atherosclerosis complain of attacks of giddiness, and it is difficult to explain this symptom, except in those patients who have a hæmorrhage into the labyrinth and complain of vertigo, tinnitus and deafness of sudden onset. The vertigo associated with cerebral hæmorrhage or thrombosis seldom provides a diagnostic problem, because this symptom is overshadowed by other more striking manifestations. The vertigo of syncopal attacks and of aortic regurgitation is explained by interference with cerebral or vestibular function by the poor cerebral blood-flow accompanying these conditions.

Disturbances of the intracranial tension are frequently associated with attacks of vertigo. This may result from interference with the cerebral circulation or from pressure on the nerve tracts.

Intracranial space-occupying lesions very frequently produce attacks of giddiness or "light-headedness", but severe rotational disorder is rare unless the tumour involves the vestibular fibres. In the cases not associated with a vestibular lesion, the general symptoms of raised intracranial tension and the focal symptoms produced by the lesion overshadow the vertigo, and a routine neurological examination, including examination of the fundus of the eye for papillœdema, will establish the diagnosis.

Attention has recently been redirected by Page to the vertigo of intracranial hypotension. Magendie in 1825 described vertigo following removal of the cerebro-spinal fluid and attributed it to cerebral anæmia due to pressure on the basal blood vessels by a brain which is no longer supported by its cushion of cerebro-spinal fluid. This condition may occur as a result of continued leakage of cerebro-spinal fluid after lumbar puncture or head injury. Thus, some of the cases of continued headache, vomiting and vertigo after head injury may be due to continued leakage of cerebro-spinal fluid, but it should be remembered that the labyrinth itself is very susceptible to injury.

Ocular Vertigo.

Vertigo may occur as a result of unusual visual perceptions, such as looking down from great heights or looking into a swinging mirror. This occurs because we are accustomed to balancing ourselves by the combined action of visual and labyrinthine impulses, so that, if visual stability is impaired by removing concrete, stationary objects, upon which we may focus our eyes, unsteadiness of balance results.

Pathological ocular vertigo occasionally occurs as a result of paralysis of the external ocular muscles, because there is false projection of the visual fields, so that the patient wrongly judges the relationship of his body to what he sees. In such cases the vertigo is not severe, and the ocular symptoms, such as diplopia, are so obvious that the diagnosis is not difficult.

Vertigo Associated with Lesions of the Brain-stem.

Lesions of the brain-stem frequently produce vertigo, because damage to the vestibular nuclei and vestibular tracts, both ascending and descending as well as those passing to and from the cerebellum, may occur. Since the cranial nerve nuclei and the tracts of the brain stem are compressed into a relatively small space, lesions of the brain-stem which produce vertigo are associated with lesions of the cranial nuclei and the nerve tracts, so that striking neurological abnormality is produced. A full neurological examination will therefore establish the site of the lesion or the site of the pressure effects produced by a lesion of nearby structures.

Sudden severe vertigo, often associated with the violent throwing of the patient to the ground, together with vomiting and dysphagia, is produced by thrombosis of the posterior inferior cerebellar artery, giving rise to the lateral bulbar syndrome or cerebellar apoplexy. This artery supplies the lateral aspect of the medulla and the under-surface of the cerebellar cortex. Infarction of these areas produces ataxia of the ipsilateral limbs from inter-

ruption of the cerebellar afferent fibres of the *corpus restiforme*, unilateral nerve deafness, vertigo and nystagmus from involvement of the vestibular and cochlear nuclei, loss of pain and thermal sense of the side of the face on the side of the lesion from involvement of the sensory nucleus of the trigeminal nerve, paralysis of one side of the pharynx and soft palate and one vocal cord on the side of the lesion, due to affection of the *nucleus ambiguus*, and loss of pain and temperature sensibility of the contralateral limbs and trunk from interruption of the spino-thalamic tract. Light touch is intact because the touch fibres in the medial lemniscus are not involved. Ipsilateral hypoglossal paralysis resulting in deviation of the tongue to the side of the lesion is often present, and Horner's syndrome may occur on the side of the lesion, being due to interruption of the sympathetic fibres in the *formatio reticularis*. There is seldom interference with pyramidal function.

Thrombosis of other arteries supplying the brain-stem seldom produces vertigo, because the vestibular connexions are not affected.

Tumours of the brain-stem and the fourth ventricle produce vertigo less often than would be expected, probably because the destruction of vestibular connexions occurs gradually. Tumours of the brain-stem produce symptoms and signs of localizing value, and, in addition, evidence of obstructive hydrocephalus appears early in about half these cases.

Other lesions of the brain-stem may produce vertigo, and the more acute the process, the more likely is vertigo to result. Vertigo is not a common symptom of disseminated sclerosis, but occurs when a plaque of the disease involves the vestibular connexions. Because of the slow progression of the pathological process, vertigo is rare in syringobulbia.

Cerebellar Lesions.

Cerebellar tumours are associated with vertigo in only about 50% of cases. This is surprising when one considers the intimate connexion of the cerebellum with the vestibular apparatus and also the fact that so many cerebellar tumours are associated with raised intracranial tension.

It is stated that intracerebellar tumours of the lateral lobe may produce a form of vertigo in which the subjective sense of rotation of the body is in the same direction as the apparent movement of surrounding objects, that is, away from the side of the lesion. In extracerebellar tumours of the cerebello-pontine angle, while external objects appear to move away from the side of the lesion, the sense of subjective rotation is reversed, that is, towards the side of the lesion (Purves-Stewart, 1952).

If the vertigo is due to a cerebellar tumour, there will be other signs of cerebellar disease—nystagmus, hypotonia, incoordination of movement, past-pointing *et cetera*. There is usually evidence of raised intracranial pressure.

Vertigo is not a common symptom in the cerebellar atrophies, probably because of the slow progression of the disease process.

Tumours of the Cerebellar-Pontine Angle.

An acoustic neuroma is a tumour arising from the eighth nerve, but its most characteristic effects are produced by pressure on surrounding structures. The first symptoms to appear with eighth nerve tumour are usually tinnitus and deafness, and these symptoms are probably related to interference with fibres in the nerve itself. Vertigo and nystagmus appear later and are probably caused by pressure on the central vestibular connexions. Other effects of pressure on the brain-stem and cranial nerves occur later. Thus sensory loss in the trigeminal distribution and, particularly, loss of the corneal reflex, and facial paresis, both on the side of the lesion, occur. There may be diplopia, due to involvement of the sixth nerve. Compression of the cerebellum causes cerebellar symptoms on the side of the lesion, and compression of the brain-stem may cause interruption of either pyramidal tract. There may be reduction or loss of response to caloric stimulation on the side of the lesion. The protein content of the cerebro-spinal fluid is almost always raised, and the radiographic demonstration of widening of the internal auditory meatus is a valuable and diagnostic sign.

Other tumours of the cerebello-pontine angle may cause similar symptoms. A meningioma may grow in this area, but this tumour does not produce the same rise in cerebro-spinal fluid protein content. Arachnoiditis, particularly loculated arachnoiditis, involving the cerebello-pontine angle and causing pressure on the eighth nerve, brain-stem and cerebellum, may produce effects indistinguishable from those of eighth nerve tumour, including raised cerebro-spinal fluid protein, but there is no widening of the internal auditory meatus.

Vertigo due to Lesions of the Vestibular Nerve.

Eighth nerve tumour has already been discussed.

Certain toxins and therapeutic agents cause vertigo. The most important substances, from this point of view, are tobacco, alcohol, salicylates, quinine, streptomycin and dihydrostreptomycin.

It is well known that tobacco, especially in the uninitiated, may cause vertigo, associated with vomiting, pallor and sweating. The youth who sneaks out into the cold night air, smoking his father's cigar, is the subject most affected. Chronic heavy smokers may also complain of attacks of vertigo.

Alcohol may produce intense vertigo. Some of us may remember that syndrome associated with excessive imbibing in which sleep is difficult because the bed leaps up and down in space when the eyes are closed.

Salicylates and quinine typically produce tinnitus and deafness, but vertigo may also occur.

The occurrence of vertigo after the administration of streptomycin is well known. The symptom is not usually of the very severe variety, and it occurs, naturally, most frequently when large amounts of this antibiotic are given over long periods. In nearly all cases the vertigo and unsteadiness disappear in time, probably because the patient learns to compensate for the damage to the vestibular system. Although dihydrostreptomycin also causes vertigo, the main brunt of its toxic effects falls on the cochlear system and deafness results. This seriously limits the usefulness of this drug, because the deafness is permanent.

Other less commonly encountered toxins, such as arsenic, mercury and thallium, may cause vertigo.

The site of the lesion produced by these toxins is not definitely known, but it is thought that most of them cause degeneration of the vestibular nerve or nuclei. The toxic effects of streptomycin have been studied intensively, and although many think it is the vestibular nerve which is affected, Ruedi has shown that, in animals, streptomycin first affects the peripheral vestibular apparatus, and he has used this antibiotic to treat patients suffering from Ménière's disease.

Peripheral Vertigo.

Peripheral vertigo will be discussed by Dr. Mackay, together with the tests of labyrinthine function.

Treatment of Vertigo.

Since vertigo is a symptom, its treatment is that of the disease causing the symptom. The symptomatic treatment of vertigo with drugs of the antihistamine group does not produce spectacular results.

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ISONICOTINIC ACID HYDRAZIDE IN PULMONARY TUBERCULOSIS.

By R. MUNRO FORD,
Adelaide.

IN February, 1952, considerable excitement was created by announcements in the American Press concerning the beneficial effects of isonicotinic acid hydrazide used in the treatment of tuberculosis. These reports claimed remarkable improvement in many hopeless cases of this disease, and photographs were even published showing patients who had all been previously assured of an early death dancing in the corridors some weeks after commencing treatment with the drug.

Medical reports concerning experimental and clinical results of the treatment with this drug soon followed.

Isonicotinic acid hydrazide was first synthesized by Meyer and Mally in 1912, and later it was used as an intermediate in the production of isonicotinaldehyde thiosemicarbazone, a compound investigated by Grundberg and Leiwert in 1951 in experimental tuberculosis. In common with related compounds, however, viable tubercle bacilli were still obtained from animals after such treatment, even in cases in which no gross lesions could be demonstrated; thus further attempts were made to isolate a more effective fraction. In 1951 Grundberg and Schnitzer (1952), Bernstein and co-workers (1952) and also Steeken and Wolinsky (1952) investigated the anti-tuberculous effect of isonicotinic acid hydrazide (INH) in experimental animals.

These works demonstrated that isonicotinic acid hydrazide ("Rimifon") and its isopropyl derivative ("Marsilid") produced dramatic beneficial effects in mice, guinea-pigs and rabbits infected with virulent tubercle bacilli. They also noted that rabbits treated with INH after intravenous infection with highly virulent bovine tubercle bacilli remained well and failed to develop miliary pulmonary lesions, but that ten weeks after cessation of the drug all showed relapse of their tuberculous disease.

Early in 1952 Robitzek, Selikoff and Ornstein (1952) published the results of treatment with INH of 92 patients suffering from pulmonary tuberculosis, 60 from far advanced disease and 23 from moderately advanced disease. Their findings were briefly as follows: (i) Elimination of fever and toxic effects within two or three weeks in all cases; (ii) an average gain in weight of 18 pounds over nine weeks; (iii) negative sputum findings in 25% of cases; (iv) complete or almost complete elimination of cough and expectoration in two to three weeks; (v) visible radiological improvement, but not nearly so dramatic as the clinical progress. They also noted relief of tuberculous laryngitis, otitis and glossitis, very few side-effects, and little clinical evidence of the development of drug resistance.

These workers continued their studies, and in January, 1953 (Robitzek *et alii*, 1953) published further evidence of the efficiency of this drug during treatment of nine to thirty-four weeks' duration. They also suggested that, although the isopropyl derivatives of INH ("Marsilid") were more beneficial than INH ("Rimifon"), toxic effects, in the forms of reduced blood hæmoglobin levels and central nervous system and autonomic nervous system side-effects, were more severe with the former drug. They found that radiological improvement was slow in appearing and was not noted in a significant number of cases until three to five months after treatment had been commenced, cavity closure and clear-cut clearing of exudative lesions being most prominent. In addition, little evidence of in-vivo or in-vitro development of drug resistance was noted.

Various other reports concerning the efficacy of these compounds against tuberculosis soon followed (Steenken *et alii*, 1952; Veterans Administration, 1952), and most of these findings show that the beneficial clinical results were rather less than those described by Robitzek and his co-workers; that radiological response appeared rather less satisfactory than that following treatment with streptomycin *plus* PAS in similar types of disease; and also that at least in-vitro resistance to the drug did develop during treatment at rather an alarmingly rapid rate.

In October, 1952, a report was issued by the Medical Research Council of the Privy Council comparing the efficacy of INH with that of streptomycin *plus* PAS over a three months' period of treatment in various types of pulmonary tuberculosis. Their conclusions were that INH was a very effective drug in pulmonary tuberculosis, but that given alone it was not more effective than streptomycin *plus* PAS. Bacillary resistance to INH was found in 11% of cases at the end of the first month, in 52% at the end of the second month and in 71% at the end of the third month; worsened clinical and radiological response was related to the development of such in-vitro resistance.

Proust and others (1953) recently reviewed the treatment of 20 patients suffering from pulmonary tuberculosis with INH, all of whom were streptomycin-resistant. These showed good clinical improvement in all cases, persisting positive sputum findings in 13 cases and generally poor radiological response, some improvement being shown in seven cases.

Witkind and Willner (1953) investigated the effect of INH in 20 cases of pulmonary tuberculosis, 12 of far advanced disease, during five to fifteen weeks of treatment. These results were less dramatic than those of Robitzek and his colleagues; but they indicated that INH primarily combats the systemic toxins, and to a much lesser extent the local lesions observed in tuberculosis. Witkind and Willner observed that the degree of radiological improvement in these cases did not compare favourably with that following treatment with streptomycin *plus* PAS.

As had previously been pointed out by Bosworth and his co-workers (1952), Witkind found that one of the most impressive beneficial effects of the drug occurred in the rapid healing of draining tuberculous sinuses.

Krieser and his co-workers (1953), using INH in the treatment of pulmonary tuberculosis occurring in psychotic patients, found that the mental condition improved in a reasonably high percentage of cases; one patient suffering from attacks of Jacksonian convulsive seizures who died from these during treatment with INH has been reported (Fetterhoff *et alii*, 1952).

Perkins (1952) emphasized the following points in INH chemotherapy of tuberculosis: (i) The drug has been found to be effective against tubercle bacilli in the test tube and in tuberculous infection in experimental animals. (ii) If treatment is continued for only three to four months in such experimental animals and then discontinued, relapses occur. (iii) Virulent tubercle bacilli have been grown from small residual pulmonary lesions removed at autopsy on experimental animals which were killed after having apparently recovered following intensive and prolonged treatment with the drug. (iv) Strains of tubercle bacilli which are resistant to the action of the drug appear in the sputum of the patients under treatment. (v) The best effect of the drug was noticed clinically. (vi) Apart from its cheapness, lack of toxicity and easy administration, it seems doubtful whether from a purely therapeutic standpoint isonicotinic acid hydrazide will prove to be greatly superior to the already very effective combination of streptomycin and PAS.

Joiner and his colleagues (1952) published the results of a trial comparing the effectiveness of INH alone and in combination with streptomycin against pulmonary tuberculosis. They found that, used alone, INH produced a beneficial effect in far advanced disease during the first three to six weeks of treatment, but after this deterioration usually occurred and was associated with the development of drug resistance. These findings were mostly based on changes in weight, blood sedimentation rate and bacillary content of sputum. However, when streptomycin was used with INH they found that this beneficial effect was maintained for at least eighteen weeks.

THE PRESENT INVESTIGATION.

The present trial has been carried out at the Morris Hospital, Adelaide. Twenty-five patients suffering from pulmonary tuberculosis and receiving treatment with isonicotinic acid hydrazide ("Rimifon") have been reviewed at three and six months after the commencement of treatment.

All received 200 to 300 milligrammes of INH daily in two doses, 22 also received PAS (12 grammes daily in four divided doses), and the remaining three received streptomycin, two grammes three times a week. Complete bed rest was continued in each case and no collapse therapy was instituted in any case.

Twenty-one patients had previously received streptomycin *plus* PAS with no therapeutic benefit. All of these patients had developed a recent spread of their disease. All had unilateral or bilateral cavitation, and in five this was "tension like" in nature. Four patients in this category were suffering from acute tracheobronchial or laryngeal tuberculosis.

Of the four patients who had not been treated previously by chemotherapy, three had bilateral exudative disease of probably recent origin, and one, a girl, aged ten years, had unilateral disease with tuberculous endobronchitis.

Each patient was assessed prior to and during treatment in the following manner: (i) Daily recording of (*a*) temperature, (*b*) cough, (*c*) amount of sputum, (*d*) urinary findings; (ii) weekly estimation of weight; (iii) monthly investigation of (*a*) blood sedimentation rate, (*b*) complete blood picture, (*c*) radiological changes in the chest. Sputum and gastric lavage resistance tests were carried out at the completion of treatment.

Results of Treatment.

Clinical Observations.

During the first two weeks of therapy 22 patients said that they felt a lot better and had improved appetites. Even three patients not included in this study, who died a few days after commencing INH treatment, insisted that they were feeling much better despite their obvious clinical deterioration.

During the third and fourth months of treatment seven patients said that they were again commencing to feel poorly. This number increased to 13 at six months and included two of the three patients receiving INH *plus* streptomycin.

Twelve patients had high "swinging" temperatures, and all the others had slightly elevated temperatures (99° to 100° F.) on commencement of therapy. Of the former, the temperatures of five returned to normal and those of five were reduced within a few weeks; this followed the pattern of streptomycin *plus* PAS therapy. In all, at three weeks, 18 patients had relatively no pyrexia. It was noticed, however, that of these eight had elevated temperatures again at the end of six months.

Thus, at the end of six months, only 10 patients were apyrexial.

Weight.—Weight changes were not startling, only two patients, who were inclined to obesity, showing any great increase. An average of seven pounds was gained during the first two months; this was unaltered over the next two months, and a slight average drop (one pound) was noted during the fifth and sixth months of therapy.

Cough and Sputum.—Soon after the commencement of therapy, cough was decreased in 15 cases and the amount of sputum in 11; however, during the last three months of therapy cough and sputum gradually increased again in 13 patients. Seven patients at the end of six months had lost their cough and sputum completely.

Blood Sedimentation Rate Changes.—Prior to INH therapy, the average blood sedimentation rate was 27 to 42 millimetres in one hour. At the end of three months the figures were 10 to 25 millimetres in one hour, and at the end of six months they were 23 to 39 millimetres in one hour. This shows a return to a higher level during the last few months of treatment. The patients with the most severe toxic effects showed the most mobile changes—the blood sedimentation rate nearly always dropped sharply a few weeks after the commencement of therapy, but in 11 cases returned to almost pre-treatment levels during the four to six month period of therapy.

Summary of Clinical Picture.—The overall clinical picture associated with the use of isonicotinic acid can be summarized as follows. Initial improvement occurred during the first few weeks; this state was maintained for the next two months; but after three months of therapy, in 14 out of the 22 in the "INH *plus* PAS" group and in two of the three in the "streptomycin *plus* PAS" group, deterioration occurred almost back to the level found prior to the commencement of therapy.

Sputum Conversion.

Twenty-one patients had positive sputum findings at the start of INH therapy. At three months, eight had some sputum, and in all cases it yielded positive findings. At six months, 14 had some sputum, and in all cases it yielded positive findings.

Drug Resistance.

Unfortunately it was not possible to make INH drug-resistance tests prior to therapy, but after six months of treatment all patients who had sputum containing tubercle bacilli produced highly drug-resistant organisms in amounts up to 20 microgrammes per millilitre. These included one patient receiving INH *plus* streptomycin.

Toxic Effects of the Drug.

Two patients developed signs and symptoms of toxic hepatitis, which cleared a few days after the withholding of therapy.

Two patients developed severe frontal headaches, which were relieved by antithistamine drugs.

Otherwise the toxic effects of the drug were nil.

Radiological Response.

Three patients with bilateral exudative disease of probably recent origin, who had not received previous chemotherapy, were given INH *plus* PAS. At the end of three months very slight radiological change was noted despite clinical improvement in all cases. Two patients continued this treatment for a further three months, with only slight clearing of their infiltration. In one case, streptomycin (two grammes three times a week) was substituted for INH, and the radiological improvement at the end of a further two months was good (Figures I to III).

One patient, a girl, aged ten years, had received sulphonamide, penicillin, aureomycin and "Chloromycetin", at intervals over the preceding two months, in an effort to combat a persistent cough with a daily evening pyrexia to 104° F. and continued loss of weight. A three-week culture of her gastric contents produced a virulent growth of human tubercle bacilli, which were later found to be highly resistant to streptomycin. Her chest skiagram then showed a left hilar infiltration with probable involvement of her mediastinal glands. She was given streptomycin, PAS and INH without early benefit in her clinical condition. When she was admitted to this hospital, bronchoscopic examination revealed probable endobronchial involvement, and PAS therapy was discontinued. Her clinical condition improved rapidly, she gained 10 pounds in weight, and her pyrexia subsided to an occasional rise in temperature to 99·6° F. A further chest X-ray film taken two months after the commencement of INH therapy revealed a spread in her right upper zone. PAS had been substituted for streptomycin shortly before this. Culture of her gastric contents yielded no tubercle bacilli at this stage.

Twenty-one patients had chronic disease, in most cases combined with recent exudative processes. All showed some radiological evidence of cavitation.

Good radiological improvement was noted in seven cases in which treatment was by INH *plus* PAS. This improvement was seen after one month and maintained up to three months, but in five of these cases considerable advance of

the disease, especially in the extent of cavitation, occurred during the fourth to sixth month of therapy. One patient was receiving INH *plus* streptomycin.

Eleven patients showed only slight radiological improvement or no change in the appearances at three months, and of these six had regressed further at six months.

Three patients showed considerable continued radiological deterioration during therapy.

Six of the above-mentioned patients had cavitation which was "tension-like" in nature; four of these also had coexistent laryngeal or tracheo-bronchial disease. In this group four received INH *plus* PAS and two INH *plus* streptomycin. In all cases the initial radiological improvement was remarkable, and also the laryngeal and bronchial trees became normal within two months in each case. All had previously failed to respond to streptomycin *plus* PAS therapy. However, between three and six months after the commencement of therapy four of the cavities returned to their former size or became larger than before, and in three cases bronchial involvement recurred (Figures IV to IX). One patient receiving INH *plus* streptomycin has maintained the improvement over six months (Figures X to XII).

The overall assessment of radiological changes has been as follows. Only slight improvement occurred in recent exudative types of the disease. INH *plus* PAS was not comparable with streptomycin *plus* PAS used in the treatment of other patients with similar disease. Of patients with acute on chronic disease, with cavitary elements present, seven showed considerable improvement during the first three months of therapy, but when the position was reviewed after six months, only two patients out of 21 treated had maintained good improvement; one of these was receiving INH *plus* streptomycin.

Considerable radiological improvement appeared to be related to control of endobronchial disease associated with cavitation which was "tension-like" in nature. Such improvement, however, was rarely maintained for longer than two or three months.

Straight-out deterioration in the radiological status of the patient occurred several times, despite apparent clinical benefit from INH.

Discussion.

This trial, although small, has been mainly carried out on selected patients, most of whom had reached the end of their therapeutic road. Twenty-one patients continued a regime which had failed to influence their disease favourably, except that to this regime was added oral administration of isonicotinic acid hydrazide.

Clinical changes were generally good during the first two months of therapy, with lessening of toxic symptoms, an increased desire to eat, an average gain in weight of seven pounds, a reduction in cough and sputum, and an average lowering of the erythrocyte sedimentation rate.

Toxicity was slight, and the condition of a considerable proportion of patients which was hitherto radiologically deteriorating improved considerably over this initial period.

In general, the above-mentioned beneficial effects appeared not so dramatic as those given in many previous reports, but even so it seemed that in isonicotinic acid hydrazide we had a drug which gave hope of effecting at least arrest of the condition in many cases of pulmonary tuberculosis in which the previous outlook had been hopeless.

Previous chemotherapy experience, especially with streptomycin, had taught us that if possible (*a*) bactericidal doses of any drug should be given, and (*b*) it should be used synergistically with another antituberculous drug. By this means, the emergence of that dreaded state in-vivo drug resistance appeared to be at least delayed. PAS was therefore given with INH in 22 cases and streptomycin in three cases to attempt to overcome this possible event.

However, the state of satisfaction with which one viewed the results after the first few weeks of therapy was short-lived, as patients commenced to develop a recurrence of their previous symptoms. Reduction in cough, in amount of sputum, in fever and in blood sedimentation rate and even gain in weight failed to continue after the first three months of therapy, and in a high percentage of cases these findings grew worse.

Laryngeal disease, which had completely cleared, reappeared; cavities which had vanished returned, as large as or larger than ever.

Out of 21 patients with acute on chronic disease, only one receiving INH *plus* streptomycin and one receiving INH *plus* PAS can be said, after six months of treatment, to have shown any improvement, at least in their radiological status.

The sputum of every patient who was coughing up any sputum at that time contained tubercle organisms which were highly resistant to isonicotinic acid hydrazide *in vitro* and almost certainly *in vivo*. One of these patients had been also receiving streptomycin.

Such a state of affairs is serious, and perhaps shows the value of isonicotinic acid hydrazide in a truer light.

In early cases of tuberculosis, especially those of an exudative type, INH *plus* PAS has appeared less effective than INH *plus* streptomycin or streptomycin *plus* PAS, so it seems that if chemotherapy is indicated, we are not justified in withholding streptomycin from these patients if organisms are sensitive to the drug. Whether it should be used in combination with INH or PAS is another matter which is receiving close attention in many trials.

An interesting case here is that of the child who was treated with INH *plus* streptomycin for recent disease, but who developed a spread of disease early during treatment. Her tubercle organisms were resistant to the latter drug, and thus the value of INH appeared negligible.

I suppose it was a natural tendency to use isonicotinic acid hydrazide in the treatment of patients who had previously failed to respond to streptomycin and PAS and who had a poor outlook. It is those very cases, however, in which streptomycin and perhaps PAS fail to exert a synergistic effect, that INH becomes most rapidly useless. Monthly drug resistance tests now being carried out suggest that this state occurs very quickly—usually within the first two or three months.

This trial has shown that a combination of PAS and INH fails to prevent early drug resistance in chronic or acute-on-chronic pulmonary tuberculosis and it is conceivable from past experience that streptomycin *plus* isonicotinic acid may only delay such an event.

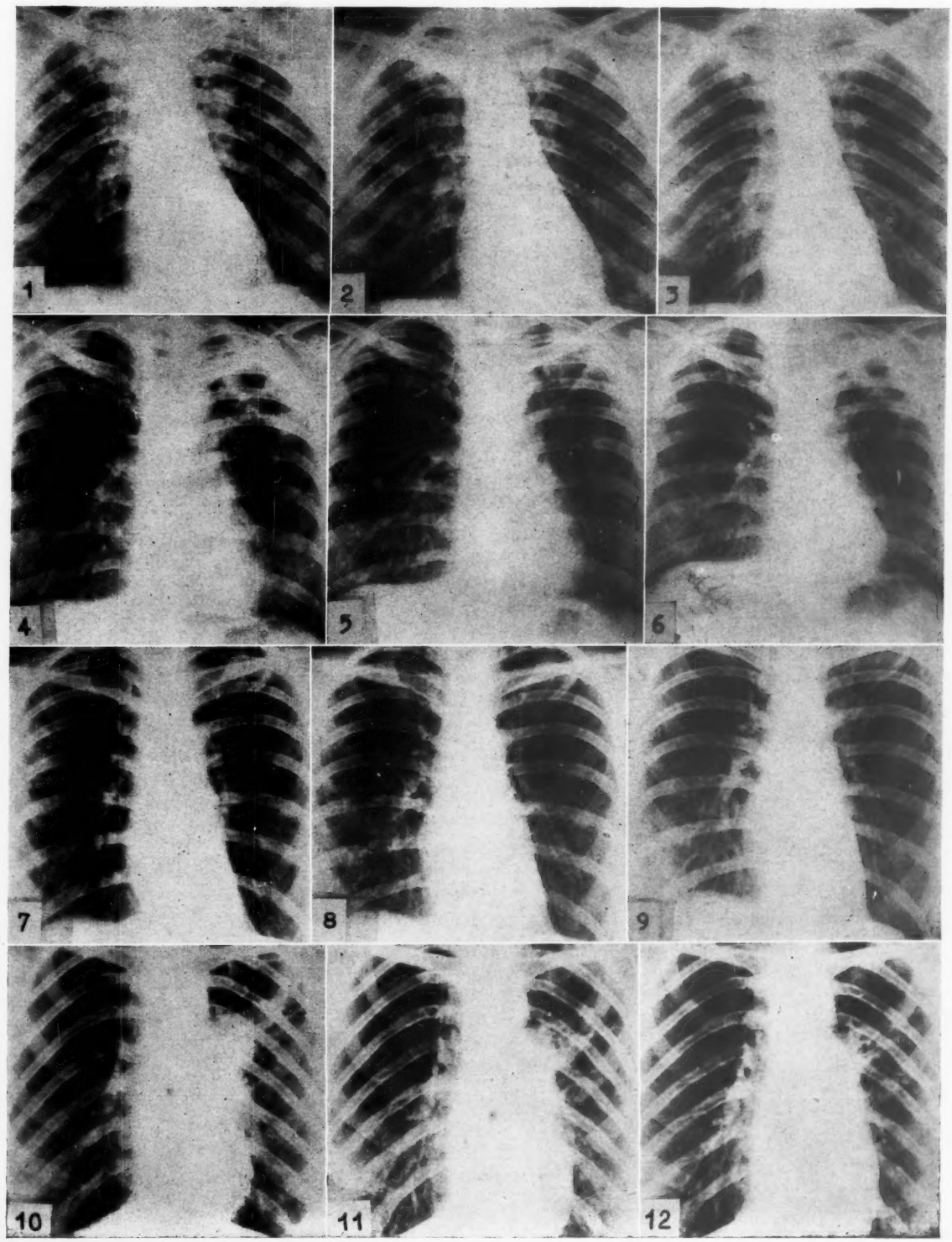
The best clinical and radiological effects of INH are seen in the first two months of therapy; it appears to boost the physical state of the patient, it clears laryngeal and bronchial disease and possibly thereby reduces the size of cavities. Such an effect seems to make the use of this drug an ideal prelude and cover to surgical treatment.

Three of these patients with previous laryngeal disease and unilateral cavitation would have been suitable cases, one month after commencement of treatment, for thoracoplasty or resection. However, their improvement was so dramatic on INH treatment that such procedures were delayed; now it is bitterly realized that as a result of the supervention of resistance to INH as well as to streptomycin, surgery has been practically excluded.

On the basis of these findings, out-patient treatment of chronic tuberculous patients with INH *plus* PAS must be condemned, as the risk of disseminating drug-resistant organisms is too great.

These findings also show how necessary it is that each case be initially carefully assessed in relation to bed rest, chemotherapy, and possible collapse or excisional measures. Unless early and adequate chemotherapy can be given in suitable cases its effect will be temporary only, and the feeling is growing that this may be the case with our present-day chemotherapy anyway. The figures of 70%

ILLUSTRATIONS TO THE ARTICLE BY R. MUNRO FORD.



ILLUSTRATIONS TO THE ARTICLE BY E. S. FINCKH, S. J. BAKER AND M. M. P. RYAN.

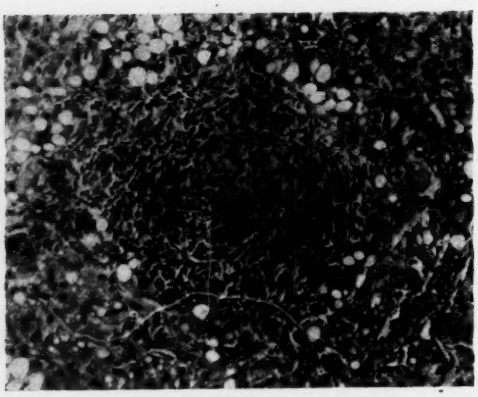


FIGURE I.

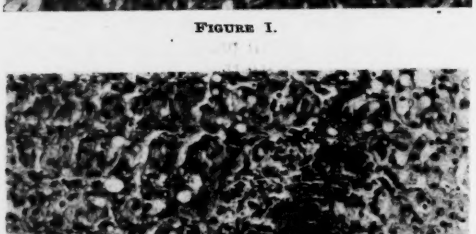


FIGURE II.

FIGURE III.

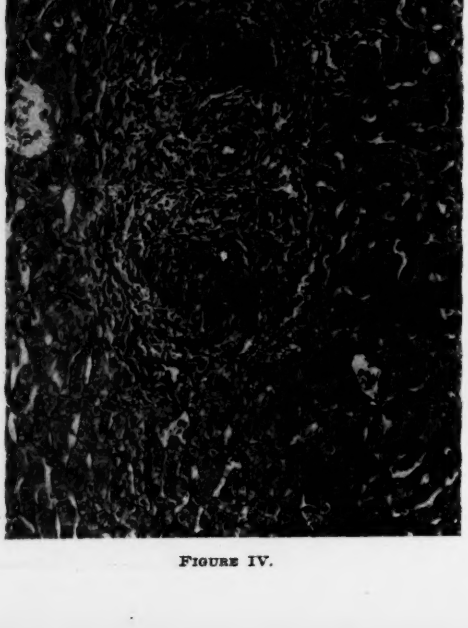


FIGURE IV.

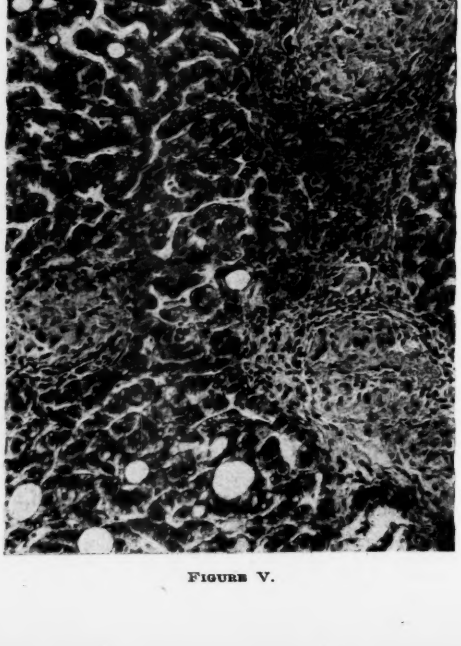


FIGURE V.

relapse rates over five years, among patients whose disease has apparently been arrested after treatment with streptomycin, tend to substantiate this.

INH could well be a valuable addition to our armamentarium of chemotherapy, especially in controlled palliative treatment and pre-operative preparation of patients. However, its administration must be carefully planned, as its effectiveness appears to last only for a few weeks.

At present we have three main drugs at our disposal—streptomycin, which is still a "must" in any active chemotherapy of tuberculosis, INH and PAS. The necessity for preventing the emergence of tubercle bacilli resistant to any of these is imperative, and is not likely to be overcome when haphazard therapy is employed.

SUMMARY.

1. Twenty-five cases of pulmonary tuberculosis treated with INH *plus* PAS or streptomycin have been reviewed; 21 cases were of far advanced acute-on-chronic disease.

2. During the first two or three months of therapy, clinical improvement occurred in nearly all cases. Radiological improvement was only slight in most cases, but in the presence of laryngeal or tracheo-bronchial disease associated with cavitation which was "tension-like" in nature, this improvement was often dramatic. Exudative processes appeared to respond less favourably than to treatment with streptomycin *plus* PAS therapy.

3. Toxic effects included headaches and acute hepatitis.

4. During the third and fourth months of therapy nearly all patients showed no further clinical improvement, and after this their condition commenced to regress. Those patients who had shown remarkable radiological improvement nearly all rapidly deteriorated during the fourth to sixth months of therapy.

5. After six months of therapy more than half the number of patients had sputum containing tubercle bacilli highly resistant to INH.

6. The implications of these findings are discussed, and it appears that PAS at least is incapable of preventing the emergence of strains of INH-resistant tubercle bacilli, especially in the presence of chronic cavitary pulmonary disease in patients who have received previous chemotherapy. The temporary beneficial effect of INH, especially on bronchial tuberculous disease, suggests that it may be useful in the preparation of the patient for surgery. An initial assessment of each patient before chemotherapy is commenced is urged.

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Legends to Illustrations.

FIGURES I, II AND III.—*An early case, in which treatment* with INH *plus* PAS was commenced at Figure I. However, at Figure II, some three months later, streptomycin supplemented INH, and the patient continued to improve even more rapidly.

FIGURES IV, V AND VI.—The patient was a woman with chronic pulmonary tuberculosis of many years' standing and recurrent tuberculous tracheo-bronchitis with left upper zone cavitation. After approximately two months' treatment with INH *plus* PAS, cavitation and tracheo-bronchitis cleared (Figure V), but recurred again a further two months later during treatment (Figure VI).

FIGURES VII, VIII AND IX.—The patient was a young girl with a history of right mid-zone cavitation occurring during a left artificial pneumothorax one year prior to Figure VII. Several previous courses of streptomycin *plus* PAS therapy gave little benefit. INH *plus* PAS therapy was commenced at Figure VII, and some three months later considerable improvement was evident (Figure VIII). A further X-ray examination some weeks after showed recurrence of cavitation in the right mid-zone despite continued treatment.

FIGURES X, XI AND XII.—The patient was a young girl with an eighteen months' history of left-sided cavitation and ulcerative tracheo-bronchitis which had previously been treated with streptomycin and PAS. At Figure X these recurred, and INH *plus* streptomycin therapy was begun. She showed remarkable improvement during the following few months (Figures XI and XII), and her tracheal disease completely cleared. She remained well, and a successful left upper lobectomy was performed some two months after Figure XII had been taken.

THE VALUE OF LIVER BIOPSY IN THE DIAGNOSIS OF TUBERCULOSIS AND SARCOIDOSIS.

By E. S. FINCKH,[1] S. J. BAKER AND M. M. P. RYAN.

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NEEDLE BIOPSY of the liver has become an accepted procedure in the diagnosis and investigation of liver disease. In many clinics it has been used principally as an aid in distinguishing between jaundice of obstructive and infective origin, although often it fails in this regard. In cases of hepatomegaly the procedure is useful in distinguishing the fatty liver of nutritional disorder and diabetes, and the enlargement due to venous congestion. Its use in suspected cases of secondary malignant disease has in our experience often eliminated the need for laparotomy. It is of value in the diagnosis of hæmochromatosis and may often be of help in the investigation of cirrhosis.

While liver biopsy still entails some definite risk to the patient, with increasing experience and meticulous care its use is justified where it may reasonably be expected to assist in the diagnosis. Valuable information may be provided more often than was previously thought, as the liver often shares in many of the pathological processes occurring elsewhere in the body. Amyloidosis, diseases of

[1] Aided by a grant from the National Health and Medical Research Council of Australia.

TABLE I.

Patients under Investigation for a Pyrexia of Unknown Origin.

Case Number, Initials.	Age, Sex.	Clinical Features.	Results of Special Investigations.	Liver Biopsy.	Final Diagnosis.	Subsequent Course.
I F.K.	69 F.	Husband died of tuberculosis six months previously. Temperature, weakness for six weeks. Examination: liver slightly enlarged.	Mantoux text: positive (1 in 1000). Chest X-ray examination normal. Sputum examinations, blood cultures, serum agglutination tests: negative. Cephalin flocculation: weak positive. Albumin/globulin ratio: reversed.	Granulomata resembling tuberculosis. Slight fatty change, no fibrosis. Guinea-pig inoculation result positive.	Miliary tuberculosis.	Considerable improvement with streptomycin and PAS.
II L.P.	21 F.	Headache, nausea, swinging temperature for two months. Papilloedema.	Mantoux test: negative. Serum agglutination tests: negative. Chest X-ray examination: bilateral hilar gland enlargement.	Granulomata resembling sarcoidosis. No fibrosis. Guinea-pig inoculation result: negative.	Sarcoidosis.	Improved a little with ACTH.
III F.O.	52 F.	Malaise, weakness, frequent colds, night sweats for six months. Anorexia, slight cough for three weeks. Liver slightly enlarged.	Mantoux test: positive (1 : 1000). Blood count: normal. Cephalin flocculation: positive. Albumin/globulin ratio reversed. Sputum and gastric lavage examinations: negative. Chest X-ray examination: diffuse mottling of both lungs.	Granulomata resembling tuberculosis or sarcoidosis. No fibrosis. Considerable irregularity of polygonal cells.	Miliary tuberculosis.	Improvement with streptomycin and isoniazid.
IV P.K.	17 F.	Recurrent fever and headache lasting seven days for past seven months. Spleen slightly enlarged.	Blood cultures: negative. Blood count: normal. Serum agglutination tests (including brucella): negative. Chest X-ray examination: normal.	Small non-specific granulomata. No fibrosis.	? Brucellosis.	Improvement with aureomycin and "Chloromycetin".
V K.McL.	17 M.	Headache, malaise, chest pain, fever for one week. Spleen slightly enlarged. small lymph nodes palpable.	Paul-Bunnell test: negative. Blood and urine normal. Mantoux test: positive (1 : 1000). Serum agglutination tests: negative. Chest X-ray examination: normal.	Occasional lymphocyte collections but no granulomata. No fibrosis.	Pyrexia of unknown origin.	Recovery without treatment.
VI G.M.	35 M.	Cough for eight years. Recurrent fever and weakness for six months. No physical signs.	Blood and urine normal. Mantoux test, serum agglutinations and liver function tests: negative. Chest X-ray examination: normal.	Normal liver.	Pyrexia of unknown origin.	Improvement without treatment.
VII J.D.	50 M.	Recurrent fever and jaundice followed by urticaria for three years. No physical signs.	Casoni, serum agglutination tests: negative. Cephalin flocculation test: positive. Serum bilirubin: eight units. Reversed albumin/globulin ratio.	Moderate fatty change, portal tracts infiltrated with fibroblasts, lymphocytes and plasma cells. Slight fibrosis. No granulomata.	Pyrexia of unknown origin.	Improvement without treatment.

the reticulo-endothelial system, sarcoidosis and chronic infections may at times be diagnosed with certainty only by the examination of biopsy material, and in many instances liver biopsy is the logical choice.

Histological examination of the biopsy material has hitherto claimed most attention, but more recently bacteriological (Rumball and Baum, 1952) and biochemical (Waterlow, 1950; Dale, 1953) techniques have been used. While biochemical (other than histological) techniques are as yet difficult to apply as routine investigation, useful information may at times be obtained by simple bacteriological procedures on such material.

It is the purpose of this paper to describe the findings in 16 liver biopsies from patients with pyrexia of unknown origin or an obscure chest lesion in whom other investigations had failed to provide a diagnosis. In addition, we record the results of liver biopsies performed for various reasons on 25 patients with known tuberculous infection, most of whom were under treatment with antituberculosis drugs.

Methods.

Liver biopsy was performed in all cases by means of a Franseen needle with the intercostal approach (King and Perry, 1948). Where possible an amount of over two centimetres of liver was obtained, if necessary by a second puncture through the same anæsthetized track. No complications were encountered in the 43 biopsies of the present series.

The material was fixed with Masson's fixative. Serial sections were cut through the bulk of the tissue and were stained with hæmatoxylin and eosin, Van Gieson and Best's carmine stains. In addition, sections were stained by the Ziehl-Neelsen technique and by the auramine-rhodamine method for examination by ultra-violet light (Gray, 1953).

At first when granulomata were seen in the sections further liver biopsy was performed in order to inoculate material into guinea-pigs. With increasing experience, where granulomata could reasonably be expected, guinea-pig inoculation was performed with unfixed material obtained at the same time as the material for histological examination. The guinea-pigs were sacrificed after six weeks and examined for tuberculous infection.

Results.

Patients Presenting with Pyrexia of Unknown Origin.

Liver biopsy was performed in seven patients under investigation for a pyrexia of unknown origin (Table I, Cases I to VII). In all, special investigations had failed to establish the diagnosis; occasional cases had slightly abnormal results from liver function tests. The liver biopsy in three cases showed granulomata which were sufficiently characteristic in appearance to indicate that the diagnosis most likely lay between sarcoid and tuberculosis. In one of these acid-fast bacilli were demonstrated, and the inoculated guinea-pigs showed the characteristic lesions of tuberculosis. Of the remaining cases in this group, two showed no relevant changes and two showed localized abnormal collections of cells of unknown significance. It is possible that further liver biopsy in the latter would

TABLE II.

Patients under Investigation for an Obscure Chest Lesion.

Case Number, Initials.	Age, Sex.	Clinical Features.	Results of Chest X-ray Examination.	Results of Laboratory Investigations.	Liver Biopsy.	Final Diagnosis.	Subsequent Course.
VIII M.B.	67 F.	Headache, pyrexia, nausea for one month. Examination: lymphadenopathy. Liver slightly enlarged.	Diffuse mottling of both lungs.	Mantoux test: positive (1 : 1000). Cerebro-spinal fluid: normal. Gastric lavage examination: negative. Axillary lymph node biopsy: tuberculosis (histology and culture).	Granulomata resembling tuberculosis. Acid - fast bacilli in section. No fibrosis. Guinea-pig inoculation result: negative.	Miliary tuberculosis.	Great improvement with streptomycin and isoniazid.
IX E.McG.	36 F.	Asthma for years. Treated in sanatorium four years previously for ? tuberculosis. Liver slightly enlarged.	Diffuse soft mottling and fibrosis, more pronounced in upper zone.	Mantoux test: positive (1 : 1000). Sputum examination: negative (10 occasions). Cephalin flocculation: negative. Albumin/globulin ratio: reversed.	Granulomata resembling sarcoidosis. Moderate fatty change. No fibrosis. Guinea-pig inoculation and culture results: negative.	Sarcoidosis.	Improvement without treatment.
X J.M.	49 M.	Shortness of breath, slight cough for five months. Loss of three and a half stone in weight in past year.	Fine granular markings throughout both lungs. Some widening of upper mediastinal shadow.	Mantoux test: negative (1 : 10). Gastric lavage examination: negative (three occasions). Albumin/globulin ratio: slightly reversed.	Granulomata resembling sarcoidosis. No fibrosis. Guinea-pig inoculation result: negative.	Sarcoidosis.	Very little improvement with ACTH.
XI P.M.	58 F.	Diabetic for ten years. Nursed in hospital next to tuberculous patient four months previously. Cough, slight temperature and sweating, evidence of congestive cardiac failure for two months. Moderate hepatomegaly.	Left pleural effusion.	Mantoux test: positive (1 : 100). Pleural fluid culture and sputum examination: negative.	Granulomata resembling tuberculosis or sarcoidosis. Slight irregular fibrosis. Guinea-pig inoculation result: negative.	Miliary tuberculosis.	Considerable improvement with streptomycin and PAS.
XII J.C.	44 M.	Cough for three years, recently worse. Treated with deep X-ray therapy for probable carcinomatosis of lungs. Developed lymphadenopathy and laryngitis. On admission to hospital: unremittent temperature, hepatomegaly, lymphadenopathy.	Diffuse mottling of both lungs.	Mantoux test: weakly positive (1 : 1000). Sputum and gastric lavage examination: negative (before liver biopsy). Sputum examination: positive later.	Granulomata resembling tuberculosis or sarcoidosis. No fibrosis.	Miliary tuberculosis.	Temporary improvement with streptomycin and PAS followed by severe exfoliative dermatitis and death. Autopsy: fibrotic miliary tubercles throughout lungs; occasional fibrotic tubercles in spleen; very few tubercles and occasional lymphocyte collections in liver.
XIII P.R.M.	41 F.	Asthma, chronic cough and sputum for nine years.	Diffuse pulmonary fibrosis most marked on right side.	Mantoux test: positive (1 : 1000). Sputum examination: negative (six occasions). Cephalin flocculation: positive. Albumin/globulin ratio: reversed.	Slight congestion of sinusoids. No fibrosis or granulomata.	Pulmonary fibrosis of unknown ætiology.	Improvement with antispasmodics and breathing exercises.
XIV R.H.	42 M.	Chronic alcoholism. Dyspnœa, malaise, high temperature six months.	Extensive patchy mottling of both lungs.	Mantoux test: positive (1 : 1000). Sputum examination: negative (six occasions). Cephalin flocculation: negative. Albumin/globulin ratio: normal.	Slight irregular fibrosis. No granulomata.	Probably pulmonary tuberculosis.	Improvement with streptomycin and PAS.
XV M.A.	67 F.	Flatulence, loss of weight, cough, fatigue for three years. Occasional chest pain. No temperature. Slight enlargement of liver.	Widespread cavitation and consolidation of both lungs.	Mantoux test: negative. Sputum and gastric lavage examination: negative. Cephalin flocculation: normal. Albumin/globulin ratio: normal.	Slight polygonal cell irregularity. No fibrosis or granulomata.	Pulmonary fibrosis and cavitation of unknown ætiology with superadded pneumonitis.	Improvement with penicillin.
XVI H.W.	44 M.	Dyspnœa for nine years, slowly worsening. No temperature.	Extensive fibrosis of both lungs.	Mantoux test: negative. Sputum examination: negative. Cephalin flocculation: negative. Albumin/globulin ratio: reversed.	Slight congestion. No fibrosis or granulomata.	Pulmonary fibrosis of unknown ætiology.	No change.

have been more informative. Two cases illustrate the help obtained by liver biopsy.

CASE I (Tuberculosis).—F.K., a female patient, aged sixty-nine years, was admitted to the Royal Melbourne Hospital in January, 1952, for investigation of pyrexia, known to have been present for at least six weeks. Some months previously her father had died of pulmonary tuberculosis. On examination the patient was a thin, miserable old lady, with a just palpable liver edge but no other abnormal findings. Her temperature ranged from 99° to 102° F. over the next six weeks. All investigations as to the cause of her pyrexia were unhelpful, including X-ray examination of the lung fields, microscopic examination of the urine, repeated blood culture, blood examination, agglutination tests, and skin and muscle biopsies. The Mantoux test result was positive (1:1000 old tuberculin) and the liver function tests showed a reversal of the albumin/globulin ratio (2·5/4·5) and a positive cephalin flocculation response. Liver biopsy showed granulomata containing giant cells suggestive of tuberculosis or sarcoidosis (Figures I and II); acid-fast bacilli were found in a Ziehl-Neelsen stained section, and inoculated guinea-pigs developed the changes of tuberculosis.

The patient was treated with streptomycin and para-aminosalicylic acid (PAS) with considerable objective and subjective improvement. Liver biopsy repeated a year later showed only some fatty change and no granulomata.

CASE II (Sarcoidosis).—L.P., a female patient, aged twenty-one years, presented at the Royal Melbourne Hospital with a two months' history of fever, headache, vomiting and dysphagia. Examination revealed a thin and rather unintelligent girl, with bilateral papillœdema but no other physical abnormality. For the next two weeks her temperature ranged from 99° to 101° F. Chest X-ray examination showed "marked hilar glandular enlargement". Microscopic examination of urine, agglutination tests, full blood examinations, repeated blood culture, Wassermann test and bronchoscopic examination all revealed no abnormality. The Mantoux test result was negative (1:10 old tuberculin). Examination of the cerebro-spinal fluid showed normal biochemical composition and four to ten lymphocytes per cubic millimetre. Liver function test results were normal.

Liver biopsy revealed granulomata suggestive of sarcoidosis or tuberculosis (Figure III). Culture and guinea-pig inoculation of the biopsy material failed to show any evidence of tuberculosis.

A diagnosis of sarcoidosis was made, and the patient was treated with cortisone, 1500 milligrammes over three weeks. There was some subjective improvement, but diminution of the pyrexia was the only objective change. Two months later she was apyrexial, but the hilar gland enlargement and papillœdema were still present.

Patients Presenting with an Obscure Chest Lesion.

Nine patients came under investigation for a chest lesion demonstrated by X-ray examination. In all, the nature of the radiological shadows was in doubt at the time of liver biopsy (Table II, Cases VIII to XVI). In four cases the liver biopsy showed no abnormality, but in five the liver biopsy showed granulomata highly suggestive of tuberculosis or sarcoidosis. In one case the finding of acid-fast bacilli in the liver section confirmed the diagnosis, but the granulomata seen in the other four cases could have been due to either condition. Although absolute distinction between these two diseases could not definitely be made on histological or bacteriological grounds, the findings were sufficiently definite to be of considerable help in determining treatment. The following are two examples.

CASE VIII (Tuberculosis).—M.B., a female patient, aged sixty-seven years, was examined at the Queen Victoria Hospital, Melbourne, in 1950, when she complained of loss of weight. The only abnormal clinical finding was a moderately enlarged liver. Chest X-ray examination showed extensive stippling in both lungs, pleural thickening at both lung bases and a discrete nodule in the lower lobe of the right lung. The Mantoux test result was positive (1:1000 old tuberculin). She was found to have mild diabetes, and a diagnosis of primary carcinoma of the lung with multiple metastases was made.

She was readmitted to hospital two years later with frontal headaches, diplopia and blurring of vision which had followed a blow on the head with a football four months previously, and more recent vomiting, photophobia and general malaise. There had been no further weight loss. Examination showed pyrexia up to 101° F., hypertension, moderate hepatomegaly, enlarged lymph nodes in the neck and the axillæ, and left third nerve palsy. The result of Wassermann and Casoni tests were negative, and the findings from serum agglutinations, full blood count and cerebro-spinal fluid examination were normal. The sedimentation rate was raised, and the Mantoux test result was positive. Chest X-ray examination showed diffuse mottling of both lung fields. Findings from repeated gastric lavage examinations were negative.

Liver biopsy revealed granulomata containing giant cells (Figure IV), and acid-fast bacilli were demonstrated by auramine-rhodamine staining. The results of guinea-pig inoculation were negative. A subsequent axillary lymph node biopsy specimen contained granulomata from which *Mycobacterium tuberculosis* was cultured.

The patient was treated with streptomycin, PAS and thiosemicarbazone with improvement. However, she relapsed and was treated with streptomycin and isoniazid. The response was very good, and eight months after her admission to hospital her chest X-ray appearances were greatly improved and her general condition was excellent.

CASE IX (Sarcoidosis).—E.McG., a female patient, aged thirty-six years, had had a chronic cough, dyspnœa and wheezing for ten years, when in 1948 a chest X-ray examination showed "acute pulmonary tuberculosis in both lungs". She was treated for five months in a sanatorium, but tubercle bacilli were never found in her sputum and she was discharged with her condition undiagnosed.

She was admitted to the Royal Melbourne Hospital four years later with dyspnœa, wheezing, and morning cough. She was obese but looked healthy. The only abnormality on clinical examination was the presence of a liver edge palpable one centimetre below the right costal margin. Chest X-ray examination showed "widespread diffuse soft mottling and fibrosis more marked in the right upper zone. Hilar shadows may be slightly enlarged". The Mantoux test result was positive (1:1000 old tuberculin). Serum protein examination showed a reversed albumin/globulin ratio (2·8/4·2).

A provisional diagnosis of sarcoidosis was made, and liver biopsy revealed granulomata highly suggestive of this disease (Figure V). The results of guinea-pig inoculation were negative.

Only symptomatic treatment was given, and she was still well eight months later.

Hence, of the 16 cases investigated, granulomata resembling sarcoid or tuberculosis were seen in the liver biopsy in eight. Of these eight, bacteriological investigation of the biopsy material showed two to be definitely tuberculous. In three the absence of necrosis and giant cells and the orderly grouping of rather swollen epithelioid cells suggested that sarcoid was the more likely diagnosis; and in the remaining three necrosis was again absent, but the presence of giant cells and the more varied cell picture gave an appearance which could equally well have been sarcoid or tuberculosis.

Patients with Known Tuberculosis.

Liver biopsies were also performed on 25 patients with proven tuberculosis. Sixteen of these were patients with pulmonary tuberculosis of between one month's and five months' duration who were undergoing sanatorium treatment; the biopsy was carried out as part of an investigation on the toxic effects of the antituberculosis drugs being administered (streptomycin, PAS and thiosemicarbazone). It is of interest that the only patient in whose liver biopsy specimen granulomata were found was very ill at the time of biopsy and was not responding to treatment with streptomycin and PAS. An incidental finding in this group was that a number of biopsies showed fatty change and some vacuolated nuclei in the polygonal cells.

The remaining nine patients comprised seven suffering from pulmonary tuberculosis, four of whom were receiving treatment with antituberculosis drugs, and two suffering from constrictive pericarditis who were not receiving such treatment. However, only one patient was still showing evidence of considerable tuberculous activity at the time of biopsy; she was not responding to treatment with streptomycin, PAS and thiosemicarbazone. Again it is of interest that the liver biopsy specimen in this case was the only one in which granulomata resembling tuberculosis were found, and the case is described.

CASE XXXVII (Tuberculosis).—E.S., a female patient, aged thirty-six years, had spent five months in a sanatorium in

1943 for bilateral pulmonary tuberculosis. Three years later she was treated for paraplegia caused by tuberculosis of three thoracic vertebræ and recovered after three years in hospital; on her discharge in 1949 her chest X-ray examination showed appearances considered to be quiescent.

Nine years after her initial illness she was admitted to the Queen Victoria Hospital, Melbourne, in a cachectic state and with a pyrexia ranging from 99° to 103° F. Apart from gross kyphosis the only abnormal physical findings were a palpable right kidney and a moderately enlarged liver. The Mantoux test result was positive (1:1000 old tuberculin), and liver function test results were normal. X-ray examination of the spine showed reactivation of the tuberculous osteitis, and scarring. Chest X-ray examination showed miliary tuberculosis superimposed on the old scarring.

Liver biopsy showed numerous small granulomata resembling miliary tuberculosis. The results of guinea-pig inoculation, however, were negative. Culture of urine and gastric lavage subsequently grew *Mycobacterium tuberculosis*.

The patient did not respond to streptomycin and thiosemicarbazone, and two months later developed tuberculous meningitis, confirmed bacteriologically. At this stage treatment with isoniazid was commenced, and she improved dramatically. Eight months after admission to hospital she was up and about, and chest X-ray examination showed only the old scarring of the lungs.

Discussion.

It is now well known that miliary lesions of sarcoidosis and tuberculosis occur in the liver when the disease is generalized, and there have been numerous reports in the literature of such granulomata being found in liver biopsy specimens (Gillman and Gillman, 1945; Janbon, Cazal and Bertrand, 1946; Mansuy and Seiferth, 1950; van Beek and Haex, 1943). Klatskin and Yesner (1950) reviewed the subject and emphasized that the histological distinction between the lesions of sarcoidosis and tuberculosis in the absence of caseation was difficult; in only one of their 22 cases were they able to make a definite diagnosis of tuberculosis by finding acid-fast bacilli. However, Rumball and Baum (1952) reported a case diagnosed by culture of *Mycobacterium tuberculosis* from liver biopsy material. One case of the present series, previously reported by Hurley (1952), was shown to be tuberculous by guinea-pig inoculation, and this method was chosen as the one most likely to give a positive result. In all cases in which granulomata were found, guinea-pig inoculation was therefore performed, if necessary by using material from a second biopsy. In only one case, however (Case I), was a positive result obtained. This finding is similar to that of Horowitz and Gorelick (1951), who found mycobacteria by direct smear in 14 of 20 bone marrow biopsies performed on patients with tuberculosis, but succeeded in cultivating the organism in only five cases; it appears, therefore, that the miliary type of tuberculous lesion encountered contained relatively few viable organisms. These results were disappointing, as they indicated that occasional cases might still be either sarcoidosis or tuberculosis. However, rather more definite histological appearances or response to treatment reduced this doubt to some extent.

Other granulomatous conditions, such as brucellosis, beryllosis, *erythema nodosum*, leprosy, syphilis and histoplasmosis, are said to give similar appearances (Klatskin and Yesner, 1950), but these conditions were considered to be reasonably well excluded on clinical grounds.

The literature is not clear in defining the types of pulmonary or extra-pulmonary tuberculosis in which liver lesions may be expected. Saphir (1929) found miliary tubercles in the liver *post mortem* in 80 of 100 cases of "chronic ulcerative tuberculosis", and Lorentz (1913) found lesions in the livers in 99 of 100 cases of chronic tuberculosis at autopsy, although the latter appears to have dealt mainly with abdominal tuberculosis. While it may be argued that liver biopsy is less likely to give a positive result owing to sampling error, van Beek, Haex and Smit (1949) found miliary lesions by liver biopsy in all types of chronic tuberculosis. On the other hand, van Buchem (1946) found no granulomata in the liver biopsy specimens in nine cases of active exudative pulmonary tuberculosis. It may well be that further analysis of liver and other biopsy material will demonstrate differences in the extent of dissemination according to the type and site of primary infection or to the strain of *Mycobacterium tuberculosis*. These findings may be associated with differences in clinical pattern and prognosis, and provide a guide to treatment.

In view of the finding of granulomata, probably tuberculous, in four previously undiagnosed cases in the present series, it may seem surprising that liver biopsies carried out in 25 cases of known advanced tuberculosis revealed positive findings in only two. However, in the majority of these cases extensive treatment with specific antituberculosis drugs had been given, and most patients had already shown considerable response. The two patients in whom granulomata were discovered were not responding to treatment; one died shortly afterwards, and the other responded later to different therapy. It would appear likely that effective antibiotic therapy may cause early miliary lesions in the liver to resolve, as had apparently occurred in Case XII when the liver was examined *post mortem*. Slower resolution with fibrosis may also occur naturally, and recently Schiff (1951) drew attention again to healing of granulomatous lesions of the liver as the possible cause of a type of cirrhosis.

Summary.

1. Liver biopsy was performed on seven patients suffering from pyrexia of unknown origin and on nine patients with obscure chest lesions. In eight of these patients granulomata histologically resembling tuberculosis or sarcoidosis were found.

2. Inoculation of biopsy material into guinea-pigs produced a positive finding of *Mycobacterium tuberculosis* in only one case. Acid-fast bacilli were demonstrated histologically in this and in one other case.

3. The combination of clinical picture, histological appearances, bacteriology and subsequent course enabled the diagnosis to be made in eight cases. In the remaining eight cases the liver biopsy revealed no abnormality, and in these cases the condition was still undiagnosed when the patients were discharged from hospital.

4. Liver biopsy was also performed on 25 patients with proven tuberculosis. In only two of these patients were granulomata found. However, the majority of these patients had received antituberculosis treatment.

5. Liver biopsy followed by histological and bacteriological examination is a useful additional method of investigation of patients with pyrexias of unknown origin or obscure radiological lesions of the lungs, when other methods have failed to establish a diagnosis.

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Legends to Illustrations.

FIGURE I.—Liver biopsy specimen obtained from a female patient, aged sixty-nine years, with pyrexia of unknown origin (Case I). It contains a small granuloma composed of inflammatory and epithelioid cells; the adjacent liver parenchyma shows some fatty change. Ziehl-Neelsen stain revealed acid-fast bacilli, and liver tissue inoculated into guinea pigs produced the changes of tuberculosis. Hæmatoxylin and eosin. × 135.

FIGURE II.—Another portion of the liver biopsy specimen shown in Figure I. In this area is another granuloma in which two giant cells are conspicuous. Hæmatoxylin and eosin. × 135.

FIGURE III.—Liver biopsy specimen obtained from a female patient, aged twenty-one years (Case II) who was being investigated for pyrexia of unknown origin. The biopsy shows a granuloma composed of epithelioid cells, lymphocytes, plasma cells and occasional giant cells. There is no necrosis, and the appearances are more suggestive of sarcoidosis than of tuberculosis. Van Gieson. × 135.

FIGURE IV.—Liver biopsy specimen from a female patient, aged sixty-seven years (Case VIII), in whom chest X-ray examination showed extensive stippling of both lungs. The section shows a granuloma composed of epithelioid cells and inflammatory cells; a giant cell is seen in the top of the figure. Culture of a lymph node subsequently grew *Mycobacterium tuberculosis*. Hæmatoxylin and eosin. × 135.

FIGURE V.—Liver biopsy specimen obtained from a female patient, aged thirty-six years (Case IX), in whom chest X-ray examination showed diffuse mottling of both lungs. The section shows three well defined granulomata composed of large epithelioid cells and an outer zone of fibroblasts and lymphocytes. The appearances are very suggestive of sarcoidosis. Best's carmine. × 135.

THE SOURCE OF TUBERCULOUS INFECTION IN PATIENTS OF THE ROYAL ALEXANDRA HOSPITAL FOR CHILDREN.

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THIS is an account of the attempts made to trace the source of tuberculous infection of patients at the Royal Alexandra Hospital for Children.

Between June 1, 1950, and November 21, 1952, 258 patients reacted to a Mantoux test; 180 of these were in-patients and 78 were out-patients. The test was performed as a routine in one 20-bed ward from December, 1950, to November, 1952, and as a routine for all in-patients from October to December, 1951, and from February, 1952, onwards, except for those children who were in hospital for a brief period, such as children admitted for tonsillectomy.

The Mantoux test was performed by the staff of the Pathology Department of the Royal Alexandra Hospital for Children. The tuberculin used was old tuberculin (Commonwealth Serum Laboratories) in a dilution of 1:1000, the test dose was 0·1 millilitre given intradermally, and the reaction was read after an interval of two days. When the area of palpable induration exceeded five millimetres, the test result was read as positive. Doubtful reactors were retested with old tuberculin in a dilution of 1:100.

Dr. R. D. K. Reye, Director of Pathology, the Royal Alexandra Hospital for Children, has kindly supplied the following information. Approximately 8000 Mantoux tests were performed on in-patients and out-patients of the Royal Alexandra Hospital for Children between June 1, 1950, and November 21, 1952. Between February 1, 1952, and November 21, 1952, the Mantoux test was performed on 2494 in-patients as a routine, and 78 reacted.

In this study of the 258 patients who reacted, 12 had been vaccinated with B.C.G., and six of these were migrant children. Of the other 246 patients, 213 were native-born Australian children and 33 were migrant children.

From December, 1950, an attempt was made to establish a source of infection for these 246 patients who had not been vacinated with B.C.G.

Where possible the mother of the child was either interviewed at the Royal Alexandra Hospital for Children or visited at home and asked about the possibility of exposure to infection from an adult suffering from pulmonary tuberculosis. Then, unless the family was already being investigated by the family doctor or a chest clinic, an offer was made to investigate its members for tuberculous infection; the offer was extended to others who lived with the family or who visited them frequently and to those whom the family visited frequently.

Where it was not possible to interview either of the parents, other procedures were followed. If they lived in the metropolitan area, a letter was written asking them to telephone the nursing sister or the medical social worker of the Institute of Child Health; if they lived in the country, a letter was sent to the family doctor who had arranged the patient's admission to hospital, asking him for information.

As a result of our early experience, it was suggested to the parents that they invite, at the outset, all those who we considered should be investigated; otherwise, if we proceeded from family to family, the investigation savoured of a witch hunt. Another disadvantage of a piecemeal inquiry was that it was difficult to know where to stop, and if the results were inclusive, the parents were left with a vague fear for the welfare of their other children. However, if the total investigations were planned at the outset, and if no source had been found when they were completed, then the parents were reassured that all that should have been done had been done.

We found that the majority of adults were willing to cooperate and have their chests examined radiologically and their children tuberculin-tested, especially after it was explained to them that the investigations offered the following advantages: (i) if an adult was found to be suffering from unsuspected pulmonary tuberculosis, then the child, and other children, could be protected from further exposure to infection, and the adult's disease would most likely be in a remediable stage; (ii) if no adult was found to be suffering from pulmonary tuberculosis, then that in itself was reassuring, and it was probable that the child's infection was a result of chance and that further exposure was unlikely; (iii) tuberculin-testing of other children would show if they had been exposed to infection, and arrangements could be made to investigate them.

Tuberculin-testing sometimes provided pointers to sources of infection. For instance, the father and two brothers of a six-year-old girl patient all reacted to the Mantoux test. The mother and baby sister of the patient did not react. The father was in the habit of visiting his father's home, taking with him the patient and her brothers; the mother and baby sister never visited this

home. The grandfather, later, was found to be suffering from "open" pulmonary tuberculosis.

The staff of the Chest Survey Unit of the School of Public Health and Tropical Medicine performed the tuberculin tests and radiographed the chests of the contacts. The Mantoux test was performed on 236 children and on some three hundred adults. Adult migrants were not tuberculin-tested after it was found that they nearly all reacted. The chests of 354 contacts over the age of fourteen years and the chests of 38 children who reacted to the tuberculin test were examined radiologically. The results of 49 radiographs of the chests of adults and 20 Mantoux tests of children, performed elsewhere, were made available for the purpose of this study.

The investigations were considered incomplete if any adult living in the child's home or any adult who frequently stayed in the home was not checked. Similarly, they were considered incomplete if any adult whom the child frequently went to say with was not checked.

Results.

Of the 213 native-born Australian children a probable source of infection was established for 109, no source was established for 53, and investigations were incomplete for 51. Twelve adults were found to be suffering from previously unsuspected active pulmonary tuberculosis as a result of these investigations.

Table I shows the number of native-born Australian children suffering from various manifestations of tuberculous infection, and the number for whom a probable source of infection was established. There is a marked contrast in the number of probable sources established for children suffering from tuberculous cervical adenitis and for children suffering from other clinical manifestations of tuberculosis. Whereas a probable source was established for only one of the 16 children suffering from tuberculous cervical adenitis, a probable source was established for two-thirds of the children suffering from other clinical manifestations of tuberculosis. Of children who did not suffer from a clinical manifestation of tuberculosis beyond the fact that they reacted to a Mantoux test, a probable source was established for almost half.

TABLE I

The Clinical Manifestations of Tuberculous Infection in 213 Native-born Australian Children and the Number for Whom a Probable Source of Infection was Established.

Manifestation of Tuberculosis.	Probable Source of Infection Established.	No Source of Infection Established.	Investigation Incomplete.	Total.
A. Miliary tuberculosis, tuberculous meningitis, tuberculosis of bone, primary tuberculous complex in the thorax[1]	49[2]	10	15	74
B. Tuberculous cervical adenitis	1	11	4	16
C. No clinical manifestation of tuberculous infection ..	59	32	32	123
Totals	109	53	51	213

[1] One infant suffering from a primary tuberculous complex in the thorax, tuberculosis of bone and tuberculous cervical adenitis for whom a source of infection could not be established, although the investigations were incomplete, has been entered in line A but not in line B.

[2] The organism responsible for miliary tuberculosis and tuberculous meningitis from which another infant suffered proved to be a bovine tubercle bacillus.

Thirty-one children were suffering from miliary tuberculosis or tuberculous meningitis; a probable source of infection was established for 22, no source could be established for four, and investigations were incomplete for five. A bovine tubercle bacillus was recovered from the cerebrospinal fluid of one child suffering from miliary tuberculosis and tuberculous meningitis.

Thirty-five infants under the age of two years reacted to the Mantoux test; a probable source of infection was established for 23, no source could be established for six, and investigations were incomplete for six. Thus, of infants under the age of two years a probable source of infection was established for two-thirds, the same proportion as for children of all ages suffering from a clinical manifestation of tuberculosis other than cervical adenitis.

Of the 33 migrant children a probable source of infection was established for two, no source could be established for 19, and investigations were incomplete for 12. The investigation of one family led to the diagnosis of active pulmonary tuberculosis in the father.

Discussion.

Approximately three-quarters of the families of the children who reacted to the Mantoux test were completely investigated, but far more than three-quarters of adults who were invited submitted themselves for investigation; the failure of one relevant adult to be checked made the family investigation incomplete.

The failure to establish a probable source of infection for 15 of the 16 patients suffering from tuberculous cervical adenitis suggests that some of these children were suffering from an infection caused by drinking milk contaminated with a bovine tubercle bacillus. Webster (1941), in Victoria, showed that the organism responsible for tuberculous cervical adenitis affecting children was of the bovine type in 10 of 23 specimens examined.

Chinner (1947) reported that 14 new cases of adult tuberculosis had been discovered as the result of the investigation of 401 contacts of 128 children who reacted to the Mantoux test in the Adelaide Children's Hospital, in the preceding three years. Rischbieth (1948) reported that an infecting family source was found for 85% of 47 infants under the age of two years who reacted to the Mantoux test.

The present study did not lead to the discovery of as high a proportion of adults suffering from unsuspected pulmonary tuberculosis as Chinner reported, nor was the source of infection for infants established as frequently as achieved by Rischbieth. However, the discovery of 13 adults suffering from unsuspected active pulmonary tuberculosis after investigating the contacts of 246 children who reacted to the Mantoux test, or one adult for every 19 families investigated, makes the procedure worth while.

Summary.

An attempt was made to establish the source of tuberculous infection for 246 children who reacted to a Mantoux test at the Royal Alexandra Hospital for Children between June, 1950, and November, 1952. None of these children had been vaccinated with B.C.G.; another 12 children who reacted to the test had been vaccinated with B.C.G.

A probable source of infection was established for 109 of 213 children who had been born in Australia and for two of 33 migrant children. Among the native-born children a probable source of infection was established for two-thirds of the infants who reacted to the Mantoux test and for two-thirds of the children suffering from a clinical manifestation of tuberculosis other than cervical adenitis. Of 16 children suffering from tuberculous cervical adenitis a probable source of infection was established for one only, a finding which suggests that tuberculous cervical adenitis is probably often due to infection with a bovine organism.

Thirteen adults were discovered suffering from previously unsuspected active pulmonary tuberculosis.

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Professor Lorimer Dods, Director of the Institute of Child Health, conceived this survey, and I should like to thank him for the opportunity of making it.

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GENERAL ANÆSTHESIA FOR DENTISTRY: A HAZARDOUS FIELD OF PRACTICE.[1]

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GENERAL ANÆSTHESIA for dentistry commenced with the introduction of anæsthesia as we know it, with Wells and Morton in the 1840's. It has been constantly used ever since, and any attack upon it attacks a vast wealth of tradition and experience. Nevertheless, acquisitions to our knowledge of the factors involved make it possible to attack general anæsthesia for dental purposes, not primarily on technical grounds, anæsthetic or dental, nor even primarily on statistical grounds, although reference must be made to both these aspects. The technical anæsthetic problems are familiar to anæsthetists, and are not incapable of solution from a purely anæsthetic viewpoint. The technical dental problems are in fact solved by many dental surgeons without recourse to general anæsthesia.

A patient has a fundamental claim not to be submitted by his medical or dental adviser to any unnecessary risk; he is not expected to be able to assess the risk, and the burden of this paper is that in cases in which, for paltry reasons, a general rather than a local anæsthetic is administered for a dental procedure, the patient is in fact submitted to a risk of death or illness of which he and often his professional adviser are quite unaware. Anæsthetic death in its highest incidence is not common in the experience of any one individual, and the morbidity or the mortality following inhalation of infected material may never come to the notice of those present at the original operation, so that the possible consequences of a general anæsthetic do not often present themselves to the mind of the anæsthetist. Contact with coroners' records will remind one very forcibly that death is a possible consequence of general anæsthesia. As a random example, in five years ending 1932 there were 369 deaths on the operating table in New York City (Henson, 1936).

[1] Read at a meeting of the Australian Society of Anæsthetists, Adelaide, April 23, 1953.

Coroners' records and those of the Government statistician may present difficulty as a source of specialized information, which may prove to be more patchy than one would wish; but among the male deaths in New South Wales for 1951 (the female records are not in an accessible form) there is a subject, aged twenty-three years, and in the female records for the first six months of 1952 there are two subjects, aged twenty-three and twenty-four years, all of whom met their deaths during the administration of a general anæsthetic for dental purposes, and do not come into any figures subsequently mentioned.

Such records were studied by Bowden (1949) for the Melbourne coroner's area for the years 1947-1948, and one notes that in a series of 51 consecutive deaths three were for dental extractions and the subjects were aged eighteen, sixteen and fifty-eight years. Marshall (unpublished report), taking a period of eighteen months for the Sydney coroner's area in 1934-1935, noted one dental case in a subject aged eighteen years, amongst a total of 46 deaths. There were four cases of general anæsthesia, and in one only was there any suggestion of a "poor risk" patient. This is not an unfair sample; conversation with one's colleagues, medical and dental, and study of much material published over the last twenty years reveals that death does occur from time to time in association with dental operations under a general anæsthetic. There is a striking contrast in the fact that one has not so far been told, or read, of a single instance of death following dental local analgesia, despite the fact that this is overwhelmingly the commoner practice, and notwithstanding the fact that any published figures of anæsthetic death are found to contain quite a proportion of cases of regional analgesia. For example, a survey of 50,000 unselected consecutive cases quoted by Hewer (1953) showed an immediate death rate associated with local anæsthetic methods more than double that associated with general anæsthesia. There probably is mortality in association with local injection for dentistry, but it is apparently infinitesimal; this is far from the case when general techniques are employed. The disparity between the two risks would seem able to be explained by certain general considerations.

Statistics are loaded against regional techniques by the fact that it has been the practice to use such techniques for the "desperate risks", those *in extremis* at the time of the decision to operate. Other disasters are attributable to the use of excessive quantities of the local analgesic solution or to misplacement of the injection—for example, into the subarachnoid space in paravertebral block. More than a few, in any large series, are due to error in the strength or identity of the injected solution. It may be seen that some of these possibilities do not exist in the case of a dental injection, and that the patient is protected from the ill consequences of others by the necessarily small volume of the injection. The operator who injects one drug in mistake for another is unlikely to kill with his quantity of one or two cubic centimetres, and in fact many of his colleagues do deliberately inject solutions of such an agent as cocaine for their dental work, notwithstanding the general feeling to limit its use to topical application.

Every general anæsthetic for whatsoever procedure, major or minor, carries a risk to life, and our appreciation of the nature of this risk has varied over the years. One remembers as a medical student forming the impression from one's reading that the anæsthetic agent *per se* was the factor bearing the responsibility for death: ether, one chance in 11,000 cases; chloroform, one chance in 2500 cases; and so on. No doubt the nature of the anæsthetic agent will affect the risk, but nowadays far more notice would be taken of the experience and skill of the administrator, and there would be general agreement with Paul Wood: "Given a properly trained and qualified anæsthetist, morbidity and mortality fall, regardless of the agent, technique, or patient condition." "Fall" and not "disappear" was the word used, and we should recognize that any general anæsthetic effects a substitution of fallible human care and apparatus for the reasonably infallible protection afforded to the patient by his reflexes; for instance, the larynx until it is anæsthetized repels unphysio-

logical material with extreme efficiency. Civilization has introduced the motor vehicle with considerable cost to life, and in the same way as accidents occur on the roads, so accidents may occur in association with anæsthesia. Dental anæsthesia is one means by which we may be reminded of the important general fact that anæsthesia, like surgery, is a dangerous art and should be practised only when absolutely necessary.

It is not easy to determine how great this risk is or what is the statistical probability of death occurring under an anæsthetic. Many investigators, and notably Ronald Jarman (1939), have attempted to relate the number of deaths to the total number of administrations and have found it impossible to do so from the information supplied. It would be still more impossible to feel assured that one had been furnished with particulars of the total number of deaths which might reasonably be called "anæsthetic deaths". For all the homage done to massive collections of figures, and for all the support given to Flagg's dictum that the volume of a single man's experience is too small to form a true statistical estimate for use by others, it should be borne in mind that the big figures reflect the findings of many different observers, who commonly vary profoundly in the interpretations they place upon similar sets of circumstances. The data for an expert's analysis are frequently assembled by inexperienced assistants, such as newly qualified resident medical officers, who may record conscientiously and well, but equally may fill up the blanks on an investigation sheet in accordance with their memory, imagination, or feeling of what ought to go in, long after the patient's decease. To those who may feel such cynicism to be unhealthy, the classification of risk sections of the mass Australian figures subsequently referred to will be of interest. At one major hospital, whose anæsthetic department is closely supervised by a senior colleague, just half the deaths are listed as occurring in subjects apparently healthy. Few other hospitals show more than a small proportion of their anæsthetic deaths as occurring in "first-class risk" patients. There are many instances in which acceptance of statistics would be influenced by inside knowledge of the circumstances of their collection. On the one hand it is not unknown for the consequences of ill-conceived surgery to be attributed to the anæsthesia, and on the other hand "there is a natural tendency to record successful treatment and to leave the failures unpublished". In England, for purposes of registration, a death under an anæsthetic is one occurring during an operation or before recovery from the effects of the anæsthetic (Association of Anæsthetists of Great Britain and Ireland, 1934-1935). Many people still regard the whether or no to report the case to the coroner as being demarcated by the doorway of the operating theatre. If the patient expires outside that doorway the case is not reported. *Status thymicolymphaticus* is now out of fashion, and by many not believed in at all, yet in the past it has been given and accepted as a quite sufficient cause for many, many hundreds of deaths. The more careful investigations into anæsthetic fatalities are liable to show much more credible causes, such as vomitus in the air pasasges, of which there were 13 instances in Bowden's 51 cases (Bowden, 1949), and 56 instances in the 232 deaths, considered to be anæsthetic in nature, investigated by the Committee of Investigation of the Association of Anæsthetists of Great Britain and Ireland in 1952. For reasons of human frailty no less than for medico-legal reasons it is a fair assumption that the recorded anæsthetic deaths tend to represent a minimum of those which actually occurred, and that the circumstances reported in connexion therewith are the least damning. One does not see surgical articles such as "The Time Incidence of Death following Ligation of the Right Hepatic Artery during Cholecystectomy", and similarly one does not see anæsthetic articles describing "Dental Extractions by Means of the Laryngoscope". Nevertheless, there would seem to be little doubt that anæsthetic death is reported by anæsthetists with more candour than almost any other form of medical misfortune; its probability seems to vary from time to time, from place to place, and from country to country, but by and large, for operations taking place on indoor hospital patients a figure of one per 1000 administrations seems to be about the average. Mass Australian figures collected in 1938 and presented in detail in THE MEDICAL JOURNAL OF AUSTRALIA of June 11, 1938, and mass South African figures collected in 1936 (Committee on Deaths under Anæsthesia, 1936) support this incidence. This figure for indoor hospital patients is relevant to a discussion of dental anæsthesia, because the present tendency in this country appears to be to frown to some extent on anæsthetics given to patients in the dental chair, but to believe that all will be well should the patient be taken into hospital and anæsthetized by a specialist with an anæsthetic machine, a Magill tube and a throat pack. The 2,000,000 case returns made to Jarman's investigation in 1939 showed 400,000 administrations of nitrous oxide in the dental chair with no mortality, but 14 cases of death in the theatre occurring to dental patients. One cannot but feel that some selection may have been exercised by the people making the 400,000 returns, or failing to make them, since mere conversation with a few of one's friends has produced three cases in New South Wales in which the administration of nitrous oxide in the dental chair was fatal. The experience of these few friends would not constitute by any means an exhaustive survey of the history of the administration of nitrous oxide for dentistry in New South Wales. Apart from these, casual reading of the Sydney newspapers will produce a case or two per year of death in association with the administration of a general anæsthetic in a dental surgery. Whilst in recent years there has been an improvement in understanding of anæsthetic principles, in anæsthetic techniques, in the drugs employed and perhaps in the skill of individual anæsthetists, there is little evidence indeed that the overall death rate has been influenced by these factors. As was said in 1946 by an Anæsthesia Study Commission (1947), which you will note to have been an American one, "in many surgical amphitheatres attempts to employ newer methods of anæsthesia by poorly qualified personnel have resulted in an even greater incidence of death". If there are safe techniques of anæsthesia for dental work, they ought to be capable of employment by the average practitioner, whether dentist or doctor, since there is no immediate prospect of the employment of skilled specialists for every dental anæsthetic; even if there were, it seems that we should expect a reduction in the risk rather than its elimination. There must be few experienced anæsthetists whose practice has been entirely free from unexpected disaster to a patient who was apparently a "good risk" for the procedure contemplated.

It is illuminating to give brief consideration, unscientific but very practical, to the circumstances under which not all, but many, patients subject themselves to a general anæsthetic for extraction of teeth. They arrive literally off the street, and it is in within the experience of all who have practised in this field that for all instruction to the contrary, and for all the patient's statement that he, she, or the child concerned has had nothing to eat, the stomach may contain quantities of fluid and food which is subsequently vomited. No general anæsthetic technique will afford a guarantee that such an occurrence will not occasionally lead to a fatality. The patient has to lose something of the reflex protecting his larynx before he can be intubated, and the food or fluid may precede the Magill tube into the air passages. Of the deaths studied in the investigation of the Association of Anæsthetists of Great Britain and Ireland, referred to earlier, 29% took place during induction of anæsthesia, that is, at a stage preceding an opportunity to intubate. Often there is no premedication; the fee available is not such as to encourage the permanent installation or the intermittent carrying in and out of elaborate anæsthetic apparatus. One must record having borne this last particular series of burdens up and down tortuous stairways for a few years without acquiring conviction that all hazard was thus eliminated. For the same unscientific but economic reason there may be an element of haste, an assembled number of patients to be put through. The dental operator may or may not be seized with reasonably current anæsthetic knowledge, and this has some slight bearing on the overall risk.

Books (Macintosh and Bannister, 1952; McKesson, 1935; Mead, 1935; Clement, 1949) have been written on the variety of agents and techniques possible to deal with a situation which is inherently difficult—the operation is taking place across the patient's airway, which may be subjected to obstruction, or fouling by septic inhalation. The common employment of the sitting posturé merits a little consideration. Most dental authorities state that this reduces the possibility of inhalation of fragments, but recently acquired knowledge of the effects of posture on the blood-flow to different portions of the body during an anæsthetic makes it possible to speculate whether the brain in this position would always receive a reasonable quota of blood with the employment of such an agent as thiopentone or even ethyl chloride.

No technique has been discovered which is free from certain general hazards, such as asphyxia by vomiting; and the more complicated the technique of anæsthetization is made, the more the patient comes to be dependent upon the anæsthetist's skill and upon the efficient functioning of the various pieces of apparatus. The proposition that every additional procedure introduces possible risk would appear to be a very sound one. The possibilities are almost endless: malposition or blockage of tubes, malposition of a cylinder on a machine, failure to remove a throat pack, intraarterial or perineural injection of thiopentone. Very seldom, of course, but every now and then, a new nightmare enters the lists, and professional skill has to be supplemented with a little good fortune to avoid disaster.

Should we consider a reversion to the simple and well-tried methods, such as intermittent closed administration of nitrous oxide, nasal administration of nitrous oxide and oxygen, or administration of ethyl chloride and ether, the anæsthetist then standing aside—the "smash and grab raid" so called, the technique employed in Bowden's three deaths noted earlier? If there is any need for an answer to this suggestion, it would appear to be contained in an excellent article by Heath (1937). He quotes a search of post-mortem records of patients who died under general anæsthesia for operations on the upper respiratory tract, 56% of them having blood in the lungs or air passages. Reference is made to an investigation by Myerson in 1922, of 100 tonsillectomies carried out under light general anæsthesia; 72 of the patients had blood and mucus below the larynx at the conclusion of the operation, and this finding may receive confirmation from anyone employing a laryngoscope at the conclusion in a series of smoothly conducted tonsillectomies, the anæsthetic being ether blown into the pharynx per medium of a Boyle-Davis gag. Heath quotes clinical and experimental evidence to show that foreign material is readily inspired from the oral cavity during general anæsthesia or where the pharynx is cocainized. The clinical evidence was furnished by a *questionnaire* to some 500 patients of the Melbourne Dental Hospital who had had ten or more teeth extracted under nitrous oxide. About 8% manifested respiratory sequelæ, severe enough in the case of 3% to cause them to consult a doctor. The continuous nasal administration of nitrous oxide and oxygen has quite a deal of literature to support it, and one may see films depicting administrations in which all proceeds smoothly. Those who are able invariably to reproduce these smooth conditions with such agents are to be envied, but they still have not necessarily achieved freedom from the unpleasant possibilities already mentioned. Despite its popularity, it could be further suggested, as by Marshall (1937), that the potency of nitrous oxide is so low that more or less pronounced oxygen deficiency is inevitable in its successful administration; and it is not isolated experience that an unsupplemented nitrous oxide-oxygen anæsthetic is not conducive to careful, deliberate operating within the oral cavity. It also would appear to require a degree of cooperation from the patient and in consequence to be unsuitable for use with young children. An aspect of the situation regarding these anæsthetic subjects has been well summarized by a former president of this society (Daly, personal communication). After the showing of a film in which the anæsthetization of children in the dental surgery with nitrous oxide-oxygen was made to look absurdly easy, and the use of ethyl chloride was recommended as an alternative, he said: "I do not know how one should anæsthetize these children; if they are given ethyl chloride and ether the time will come when a child will suddenly assume the colour of the flathead's belly, and the anæsthetist will wish that he had never heard of ethyl chloride." One has seen this and would add an experience of three anæsthetic convulsions in a series of some 150 children in whose cases "Vinethene" was used in a Goldman's inhaler with the bag filled with oxygen. The Goldman's inhaler is now gracing the museum of the Australian Society of Anæsthetists. Refinements can be added, but not many anæsthetists appear to practise intubation and throat-packing in small children for the removal of small numbers of teeth, and the extra safety initially could be offset by an occasional occurrence of glottic œdema. Iconoclasts habitually suffer from a failure to suggest alternatives, and the uncontrollable child with an abscessed tooth presents a severe problem. Remote nerve block of an inflamed area is within the capacity of good dental surgeons, if the child by premedication can be brought to a state where local techniques are feasible. Lack of time to devote to this, rather than lack of ability, is probably the usual obstacle.

With adults one may refine nasal administration of nitrous oxide and oxygen in the dentist's surgery to the point of adding trichlorethylene to it, intubating blindly and putting in a throat pack; or more recently, by organization of apparatus and trained assistance, one may intubate under thiopentone and succinyl choline chloride anæsthesia, pack off the throat and maintain anæsthesia with a closed circuit of nitrous oxide and oxygen. The best hospital will provide no greater element of safety than can be organized in the surgery of a cooperative dental surgeon, and one mentions experience of reasonably elaborate procedures to help dispute once more any suggestion that risk is necessarily eliminated if one conducts the anæsthesia in a hospital as against a dental surgery, or that if only such and such a technique of general anæsthesia were employed there would be no cause for alarm. No doubt greater skill and better organization can be brought to bear to reduce the possibilities of disaster in the administration of a general anæsthetic for a dental procedure, but there would seem to be some risk inherent in any general anæsthetic, not excluding those for dentistry, greater in the hands of some, much less in the hands of others, and never altogether eliminated. If all this or any substantial proportion of this be true, is it a risk which has to be taken in order that dental work may be performed, in the same way as similar risks are undertaken for purposes of ordinary surgery?

The following indications for general anæsthesia are commonly given: (i) the hypersensitivity to local anæsthetic drugs found in a small group of patients; (ii) procedures of long duration; (iii) moderately traumatic procedures; (iv) operations in extensively inflamed fields; (v) procedures in which the extent of operation is undetermined; (vi) cases requiring extensive use of cautery.

There must be some elasticity in the interpretation of these indications, because there are busy dentists who may go twelve months without making use of a general anæsthetic for a patient. If these were all accepted as regular indications for general anæsthesia, they still would not account for a majority of the general anæsthetics administered in this country to dental patients. The only indication in the majority of cases is not a clinical or scientific one, it is merely that the patient says: "My dear, I just simply couldn't bear to be conscious while my teeth are extracted", or "Ah, doctor, I must 'ave the chloroform to 'ave me teeth pulled out". It can be contended that this should not be recognized to be a sufficient indication for administering a general anæsthetic in these circumstances. If an anæsthetist's own child is to have a general anæsthetic for any procedure, it is usual for the anæsthetist to reveal his appreciation of the possibilities by taking a lively interest in the choice of the administrator. If a patient, neither belonging to our profession nor needing surgical therapy, presented to any of us and asked to be given an anæsthetic, "just to see what it was

like", he would meet with a refusal; we would decline to subscribe to an unnecessary risk. There might not be much more justification in administering a general anæsthetic for no better reason than to satisfy a dental patient's whim, in a case in which a regional technique would serve the purpose.

A practitioner (Seeman, 1944), writing to condemn roundly local analgesia for dental work, was able to list these disadvantages: ischæmia leading to infection, more swelling and pain, and slower healing, together with the possible occurrence of post-operative paræsthesiæ and neuralgias. These would seem to be rare, and a rather minor list when compared with the possibilities associated with general anæsthesia: anything from bronchitis to lung abscess, cerebral degeneration, as described by Courville (1938), or what is probably the commonest of the serious complications—immediate death.

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Reviews.

Diseases of the Ear, Nose and Throat. By J. Douglas McLaggan, C.V.O., M.A., M.B., Ch.B. (Aberdeen), F.R.C.S., and Josephine Collier, M.A., B.M., Ch.B. (Oxon.), F.R.C.S.; *Second Edition; 1952. London: H. K. Lewis* and Company, Limited. 9" × 6", pp. 446, with 149 illustrations. Price: 37s. 6d.

IN the preface to the first edition of this book the author, J. Douglas McLaggan, stated: "This book is an attempt to teach the principles of ear, nose and throat work." With that object special stress is made throughout on the anatomical side. The second edition of the book appears under the joint authorship of McLaggan and Professor Josephine Collier, and has been prepared with the needs of undergraduate medical students in mind and as a background to clinical work in the out-patient department. At the commencement of each of the four sections into which the book is divided there is a brief outline of the anatomy and of the standard methods of examining the respective regions covered by the particular section. The description of the commoner diseases is often excellent. This is particularly true of middle ear suppuration, especially the chronic forms. Other sections such as that dealing with inflammatory conditions of the auricle and external meatus are likely to prove confusing owing to an attempt to divide the inflammatory process of these parts into a number of different types without a clear description of their specific diagnostic features. No precise outline of treatment is given for these conditions. This section needs rewriting in a more practical form, for there are conditions which the general practitioner may often be called upon to treat. There is a good description of the problem of deafness and of the methods of examination and diagnosis. The commoner operations such as tonsillectomy are adequately described and rendered clear with drawings, although more details and illustrations of adenoid removal might have been included. The description of laryngeal diseases and disorders of function is well compiled and helpfully illustrated. Finally there is a good outline of the common diseases and disorders of the œsophagus. This is a pleasingly readable book, and with but a few shortcomings it will serve admirably its purpose, to help the undergraduate to understand what he sees and to appreciate the objectives of treatment and to serve as a speedily consulted reference work for the busy general practitioner. There is a complete index and illustrations are abundant and clear.

Electrotherapy and Actinotherapy: A Textbook for Student Physiotherapists. By E. B. Clayton, M.B., B.Ch. (Cantab.); Second Edition; 1952. London: Baillière, Tindall and Cox. 9" × 5½", pp. 460, with 127 illustrations. Price: 16s.

THE second edition of this book has been largely rewritten and brought up to date.

Part I, devoted to electrotherapy, describes the basic principles of the various electric currents and apparatus used in physiotherapy. In addition there is a chapter on the modern testing of normal and denervated muscle by the strength duration method and electromyography by the new valve generated muscle testing apparatus. The chapter on long and short wave diathermy has been rewritten and contains many useful diagrams. One omission is the curved drum which greatly simplifies the application of inductothermy to the cervical, shoulder and hip areas.

Part II is devoted to actinotherapy, and a full description of the production, physiological effects and indications of ultra-violet and infra-red radiation is given. The lamps producing ultra-violet rays may soon be superseded by a new type from which all rays harmful to the eye have been eliminated so that protective goggles for both patient and operator will not be necessary.

Part III is devoted to treatment. A notable omission here is that no mention is made of treatment by sound waves. Although still in its infancy, ultra-sonic treatment has a definite field of application and the physiotherapist will be required to know something of the production, application and indications of this new method of treatment.

The text is clearly written and diagrams are adequate.

Brain Surgeon: The Autobiography of William Sharpe. With a foreword by Cecil Wakeley, Bt.; 1953. London: Victor Gollancz, Limited. 9" × 5½", pp. 244. Price: 16s.

THE catchy and alluring title given to this book, which contains an unexpurgated record of intimate personal and professional experiences in the life of a neurological surgeon, immediately suggests that the story is meant to reach a wide public rather than hypercritical and stony-hearted readers from the medical profession. After happily and successfully reaching the allotted span, Dr. William Sharpe retired comfortably to his peaceful farm estate in North Carolina with a large collection of his case histories and spent his leisure hours setting down his own achievements, his views on the shortcomings of other doctors, racial discrimination, and the truth about spastic paralysis.

There is no doubt that Dr. Sharpe has a natural gift for telling good stories in a fluent and entertaining style, although many passages in his writing show the mature journalistic touch and a decided leaning toward sensationalism. There is an unmistakable vein of subtle humour running through the recital of his varied experiences; and this delightful trait is nowhere so obvious as in his description of the inexorable Presbyterian parental discipline which dominated his submissive outlook as the dutiful son of a spirited parson working ardently in the slums of Philadelphia; or in his startling revelations concerning a consuming love affair with an expert and attractive *de facto* companion of his student days—now remembered simply as "Betty". Open confession may be good for the soul, but there are times when it can be bad for the reputation.

In spite of the fact that a determined father had predestined his youngest son for the Church, Sharpe was equally determined to enter the medical profession; so he made himself financially independent by coaching at Harvard

University, easily obtained his medical qualification, then spent a considerable period in further study at Continental clinics, and returned to serve an internship with Dr. Harvey Cushing at the Johns Hopkins Hospital in Baltimore. After a long apprenticeship in general surgery he took up a surgical appointment in China, where he was able to gain practical experience in his chosen specialty of neurological surgery. On returning once more to the United States of America he proceeded to build up a large surgical connexion in New York City.

Perhaps the most impelling reason for the writing of this book was to draw widespread attention to the seemingly unsolved problem of spastic paralysis—the need for early diagnosis of intracranial hæmorrhage in the newborn, and active treatment during the first week of life by repeated lumbar puncture. However, it may be safely asserted that the dogmatic views propounded so enthusiastically by Dr. Sharpe in the medical literature of his country since 1923 are by no means compatible with modern neurological opinion and practice in this part of the world—notwithstanding the short paragraph at the end of his last chapter: "It is as simple as that."

One more feature of the book surpasses all understanding: the President of the Royal College of Surgeons of England was prevailed upon to write the foreword.

Nutrition and Diet: In Health and Disease. By James S. McLester, M.D., and William J. Darby, M.D., Ph.D.; Sixth Edition; 1952. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Proprietary, Limited. 9½" × 6½", pp. 722, with 14 text figures. Price: £4 15s.

THE sixth edition of this book is marked by the appearance of a co-author, W. J. Darby, of Vanderbilt University, Nashville. McLester has retained responsibility for the second part which deals with diet in disease, and Darby has been responsible for the first part which is concerned with nutrition in health.

The material in the first is presented under the various headings we now expect to find in books on nutrition. Thus there are chapters on the utilization of food, calorie requirements, protein, vitamins and minerals, and then several chapters are devoted to food products.

Most books written in America are mainly for Americans, so we must accept a strong bias towards American patterns of living.

A chapter on nutritional factors of lesser importance includes sections on satiety values, roughage and digestibility. It presents much new material of particular interest to the practising physician. The importance of some foodstuffs, for example, sugar and fat, in satiety is emphasized.

The outstanding feature of the first part of the book is the manner of presentation. The author has struck a happy medium between the detailed biochemistry found in some monographs on nutrition and the sketchy outline given as a prelude in some books on dietetics. This part has been written as an introduction to Part II, and so the author has endeavoured to give the minimal of basic facts necessary for the intelligent selection of diets for various diseases. The lack of detail is offset by adequate references at the end of each chapter and by indications in the text of the most suitable sources to be consulted for more details.

This is a text-book on human nutrition, and the number of references to animal experimentation is small. However, in one or two places, for example, when discussing the nutritive value of unsaturated fatty acids, the author appears to lean a little too heavily on animal work.

After consideration of the available data the author still advocates the protein requirement at 70 grammes per day per adult, even in the face of much recent evidence to suggest that the figure could be lower. The almost complete absence of discussion of diets in which a high percentage of the protein is of vegetable origin is regrettable, in view of the fact that the major part of the world's population lives on a diet with this characteristic.

Despite these minor criticisms, Part I is a well-balanced summary of existing knowledge on nutrition, and as such should be of great value to the physician who has neither the time nor the inclination for a detailed study of the subject. The small amount of biochemistry also commends the book.

The second part has been modernized with the inclusion of recent work. Each of the main group of diseases has been dealt with in a more or less uniform manner; a brief description is given of the clinical features, pathology and biochemistry, particularly those which might relate to dietary origin of the condition or treatment. Each section concludes with a list of menus. Although these have been prepared for American palates, they could with minor modifications be applied to Australian conditions.

An appendix contains extensive tables of food composition. With the increasing interest in fluid and electrolyte replacement physicians will find the tables giving the sodium and potassium content of foods useful.

The book should be of use to physicians who take more than a passing interest in their patients' diets and to dietitians.

Nasal Sinuses: An Anatomical and Clinical Consideration. By O. E. Van Alyea, M.D.; Second Edition; 1951. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" × 6", pp. 342, with 143 illustrations, some in colour. Price: £4 16s. 9d.

THE publication of a second edition of Van Alyea's book on the nasal sinuses is evidence of the useful place found by this all-embracing study of human nasal disorders. The first two chapters cover the histopathology and physiology of these parts in simple form. In the next chapter an outline of the nature of acute nasal infection is given. In subsequent chapters each of the sinuses is considered separately. Variations in anatomical features and their influence upon disease processes and in accessibility for treatment are clearly described and abundantly illustrated. The operation of intranasal antrostomy is most favourably considered where conservative measures have failed. The more radical operations are described, though rarely considered to be necessary by the author. Removal of the antral mucous membrane, except in rare instances of gross disease, is not advised since it is considered that the lining sinus membranes are resistant to the spread of infection, and usually are capable of returning to a normal condition after adequate drainage and ventilation have been established. In like manner measures are advocated which provide for the relief of obstruction of the fronto-nasal duct, with a minimum of trauma to the lining mucosa. A very full description of the anatomical variations of the ethmoid cells and of the frontal sinus openings into the infundibulum helps greatly in the appreciation of the problem of ventilation and drainage of these parts. The radical external operations are but briefly described since they are now so rarely called for. The normal anatomical arrangement and relations of the ethmoid and sphenoid cells are beautifully described and illustrated. Sinus disease in children receives a special chapter. The role of allergy and methods of investigation and treatment are concisely and adequately described. The problem of tumours of the sinuses is usefully outlined. This includes a short description of the surgical approaches for removal and irradiation. The complications of sinus disease are systematically described and the relation of sinus disease to other conditions is explained. In the final chapter there is a treatise on general therapeutic measures including antibiotics, antihistaminic drugs, nose drops, the displacement method of therapy, and physical therapy. Dr. Van Alyea has produced a very complete yet concise description of nasal sinus disease. Every ear, nose and throat surgeon will profit with its study. As a text-book for preparation for special degrees or diploma this work is outstanding.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Clinical Diagnosis by Laboratory Methods: A Working Manual of Clinical Pathology", by James Campbell Todd, Ph.B., M.D., Arthur Hawley Sanford, A.M., M.D., and Benjamin B. Wells, M.D., Ph.D.; Twelfth Edition; 1953. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 9½" × 6½", pp. 1010, with 946 illustrations, 197 in colour. Price: £4 0s. 9d.

Dr. B. B. Wells is co-author of this work for the first time. The first edition was published in 1908.

"A Guide to Human Parasitology: For Medical Practitioners", by D. B. Blacklock, C.M.G., M.D. (Edin.), D.P.H. (London), D.T.M. (Liver.), and T. Southwell, D.Sc., Ph.D., A.R.C.Sc., F.Z.S., F.R.S.E., revised by T. H. Davey, O.B.E., M.D. (Belf.), D.T.M. (Liver.); Fifth Edition; 1953. London: H. K. Lewis and Company, Limited. 10" × 6½", pp. 236, with 123 illustrations, three in colour. Price: 25s.

The first edition was published in 1931; the fourth in 1940.

The Medical Journal of Australia

SATURDAY, SEPTEMBER 5, 1953.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

TRAFFIC ACCIDENTS AND "DRIVING UNDER THE INFLUENCE".

THE problem of motor-car driving and alcoholic intoxication was well ventilated in this journal in the issue of January 24, 1942, when three important original articles and an editorial were devoted to it. The papers were read at a meeting of the New South Wales Branch, and all bore the title "Driving Under the Influence". The first was by Mr. R. Ashburner, barrister-at-law; the second was by Acting Sergeant R. Lucas, of the New South Wales Police Force; and the third was by Dr. John McGeorge, who at that time was honorary physician at the Psychiatry Clinic of the Royal Prince Alfred Hospital, Sydney. All the important facts associated with the problem were mentioned in these articles or in the editorial, but the problem is still with us. Far from becoming less, it has increased in importance in every part of the world. In every discussion on traffic accidents, several facts require consideration. First of all, the occurrence of the accidents has to be realized, together with their number, or in other words, the magnitude of the problem. The next thing to be discovered is why the accidents occur, and there then remains for consideration what means may be adopted to prevent their further occurrence. In the current issue of the journal we publish two papers which have been contributed by request. The first is by Dr. F. S. Hansman, who has been interested in the biochemical aspect of this problem for some considerable time, and the second is by Mr. A. E. Stonham, a stipendiary magistrate of Sydney, who has taken an active part in discussions about it. Most medical practitioners use motor-cars in the course of their daily work, and they are often called upon to examine persons implicated in an accident to determine whether or not they are "under the influence". Incidentally, medical practitioners, like other members of the community, may now and again enjoy an alcoholic drink, and it is important that they should know exactly what happens to alcohol when it is taken into the body and what effect it may have on that body.

Dr. Hansman begins his article with a hypothetical story, and with an account of the replies made by 150 medical men to whom he told it, and of whom he asked a certain question. Many will express surprise that his figure, 66% (in reference to the taking of two whiskies or less), is so low, but even that figure shows with what seriousness this question is regarded by members of the medical profession. Dr. Hansman appears to be justified in his conclusion that nine out of ten doctors have found from personal experience that a concentration of 40 milligrammes *per centum* of alcohol in the blood is sufficient to affect their driving, in other words, to bring them "under the influence". Particular interest should be taken in what Dr. Hansman quotes as the inconsistency of clinical examination and the wide variation between the findings of different examiners. If an examination of the alcoholic content of the blood is made by a competent examiner, there can be no doubt. There might be some difficulty in determining the habituation of a driver to the consumption of alcohol, but surely, if a person who had been involved in an accident was found to have an alcoholic blood content above the limiting figure, the onus would rest on him to prove that he could "carry his liquor" without inflicting damage. We quite approve of the last section of Dr. Hansman's paper when he gives three notes on "how to drink". We would add to it a note: "What should be done if you do drink?", and after this would write: "Don't drive a motor-car." In Mr. Stonham's paper we would draw attention to the fact that he refers to courts of law which are faced with "the drinking driver"; he is not so much concerned with the drunken driver. He states that it is not the "drunk" who is the real traffic hazard, but "the driver who is moderately influenced, so that he is deprived of that clearness of intellect and control which is so necessary in these days of traffic congestion".

The question of alcoholic intoxicants and motor-car driving is only part of the larger question of traffic accidents in general. Traffic accidents are caused by many factors. The Superintendent of Motor Transport of New South Wales has issued a statistical statement for the year ended June 30, 1952. In this statement he analyses the responsible factors and he divides them into three classes. In the first class he groups factors which are to be attributed to human failure on the part of various people. Those whom he lists are drivers of motor vehicles, riders of motor-cycles, pedal cyclists, riders of horses and drivers of horse-drawn vehicles, trams, pedestrians, passengers, parties not involved, railway employees, riders of "billy carts", tricycles *et cetera*. In his second group are factors attributed to defective equipment of motor vehicles, motor-cycles, pedal cycles, animal-drawn vehicles and trams. His third group is attributed to miscellaneous factors which comprise animals (these include animals which vehicles swerve to avoid), road conditions and the weather. In an analysis of the very interesting figures which are set out in the comprehensive table, the conclusion is drawn that human failure was the cause of over 80% of the accidents, of over 90% of the fatalities, and of over 80% of other casualties. Drivers of motor vehicles were considered to be responsible for more than half of

the accidents, and for over 40% of the casualties occurring during the year. During the year ended June 30, 1952, no less than 613,752 motor vehicles were registered in New South Wales; the number of accidents was 22,662, that of persons killed was 741, or 1·21 per thousand motor vehicles registered; the number of persons injured was 12,637, or 20·6 per thousand motor vehicles registered. It is important to note that the greatest single cause of these casualties is excessive speed.

So far we have referred to the consumption of alcohol in relation to motor-car traffic accidents and also to the problem of traffic accidents in general. In regard to the latter, Dr. Hansman, in his paper, quotes certain figures for a survey made by the Danish Committee of Road Safety, and entitled the "World's City Traffic". The figures, as bluntly stated by Dr. Hansman and set out in the report, are a heavy indictment against Sydney and Melbourne. They will well stand investigation. The figures cover the years 1950 and 1951. The number of persons killed in traffic per 100,000 inhabitants was 18·79 for 1950 in Melbourne and 22·41 for 1951. The respective numbers for Sydney were 19·34 and 21·67; for Johannesburg they were 19·19 and 19·54. As they stand the figures for Sydney and Melbourne are more than three times the average for most of the other cities of the world. The figures for Sydney are based on a population of 3,358,760, which is stated in a footnote to cover the whole of New South Wales. It is not made clear in the graph if the number of persons killed per 100,000 inhabitants covers the whole of New South Wales and not Sydney only. As a matter of fact, the figures given to this journal by the research section of the Traffic Branch of the Police Department of New South Wales agree with those quoted in the graph and are all for the whole of New South Wales. The research officer, however, points out that the figures for 1950 and 1951 for the City of Sydney alone are 9·46 and 10·37; for the City of Sydney and suburbs the figures are 19·18 and 20·98. We have not inquired into the figures given for Melbourne, but we would probably be justified in concluding that they are at least the figures for Melbourne and suburbs. There is nothing to show in the graph whether the figures given for other cities of the world are those of the cities themselves concerned, strictly defined, or whether suburban areas are included. It is of considerable importance, for we all know that city motor traffic, although heavier than it is in the suburbs, is better controlled by traffic lights and traffic police. In spite of the deception of the figures given, every reader will agree that those for the City of Sydney and suburbs are alarmingly high. The difference between city traffic and suburban traffic gives rise to serious thought. The statistical statement of the Superintendent of Motor Transport, which has already been mentioned, shows that more accidents and fatalities occurred on Saturday than on any other day of the week, and that Friday came next. The number was smallest on Tuesday. During the hours of 4 p.m. to 6 p.m. more accidents occurred than in any other two-hourly period; the number of persons killed and injured, however, was highest between 6 p.m. and 8 p.m. In favour of the view that the presence of police or traffic lights tends to diminish the numbers of accidents, the following figures may be quoted. For 1950 to 1951, 7869 accidents occurred at intersections, and for 1951 to 1952 the number was 8379. When the intersections were controlled by police, the numbers for the two periods were, respectively, 172 and 136; when the intersections were controlled by traffic lights, the numbers were 215 and 246. When there was no control by either, the numbers were 7482 and 7997. The number of persons killed during these two periods were respectively 163 and 174. The numbers for the sections controlled by police were two and three. The numbers for intersections controlled by traffic lights were two and five; when there was no control, the numbers were 159 and 166. The significance of these figures will, of course, depend on the number of controlled and uncontrolled intersections.

The question which remains has to do with what is to be done to reduce the number of accidents and fatalities. In this regard, we must remember the statement already made that human failure is the cause of the vast majority of accidents. At the outset, this discussion dealt with fatal accidents and the consumption of alcohol. The most important fact in this regard has been stated by the authors of our two special articles; it cannot be overemphasized. It is not the drunken driver who is the real menace, but the drinking driver. There is no doubt whatever that the introduction of a compulsory estimation of the blood alcohol level of persons involved in an accident, whenever there is reasonable ground for suspicion that alcoholism may be a factor, would be an advantage. Whether this test will be introduced is a matter for each State authority in Australia. In addition we believe that suitable propaganda, presented over and over again in the daily Press, propaganda by cinematograph films and by the radio and other means, would lead at least some men and women to take a right view of this matter. The prevention of accidents not connected with alcohol must also be tackled. Control by the police has been mentioned. In the Copenhagen report we read that the number of uniformed constabulary per 100,000 inhabitants for Sydney (for this we must read New South Wales) is 112·38, and the figure for Melbourne is 130·59. These figures are not high when compared with those from other parts of the world. The highest figure comes from Lisbon, 529·39, and the next from Vienna, 457·19; the figure for London is 173·84 and for New York 231·25. There is justification for an increase in traffic police and traffic lights, particularly in the suburbs. Mention should, perhaps, be made of an apparatus known as the "Tachograph", which is being introduced into Australia from Germany. It comprises a chart which is fixed to a motor truck or other vehicle in such a way that it cannot be tampered with or easily removed. It records, for a period of twenty-four hours, every stationary period, every increase and every decrease in speed, together with the times. The inspection of such a graph would immediately show what had been happening to the vehicle when an accident occurred. The graph would show, for example, whether the driver was approaching an intersection at a reasonable speed before an accident occurred, or whether he was travelling too fast. This piece of apparatus may turn out to be useful; on the face of it, we may conclude that it would be an advantage to the careful driver; the careless or the drinking driver might not look on it with favour, but his favour need not be sought in the matter. Perhaps the object to be striven for on the roads more

than any other is the cultivation of good manners. To display good manners may take a little trouble and occupy a moment or two that would otherwise be given over to speeding. Not long ago, a driver in one of our capital cities was being somewhat hasty, when the companion by his side murmured: "Death is so permanent." The immediate slackening of speed and taking of care were a tribute to his companion's temerity.

Current Comment.

GLUCAGON.

WHEN the early preparations of insulin were injected intravenously there was an initial hyperglycæmia followed by hypoglycæmia. At first insulin was thought to be responsible, but when Abel crystallized insulin it was shown that the initial hyperglycæmia was not produced by the crystalline insulin but by something remaining in the mother liquor of crystallization. Not much attention was paid to this until Scott in 1934 crystallized insulin by a new and simpler method and this insulin produced the glycogenolytic effects. No detailed investigation of this phenomenon was undertaken for some years, although several workers noted the fact that some samples of insulin produced hyperglycæmia and others did not. From 1945 onwards de Duve and his co-workers at the University of Louvain have made a continuous study of this phenomenon and of the impurities in some samples of insulin which caused it. Quite early the active substance from the pancreas was called "glucagon". More recent workers have called it "hyperglycæmic glycogenolytic factor", H.G. factor or H.G.F. A number of American workers have also studied the phenomenon, particularly Olsen and Klein, Sutherland and Cori, Marks and Young, and Thorogood and Zimmermann.

Chr. de Duve in the Banting Memorial Lecture of the British Diabetic Association has given an historical summary of the work and details of recent work from his department.[1] The separation of glucagon from insulin has proved difficult because the two substances are very similar chemically. They are both polypeptides and de Duve has recently isolated a partly crystalline material which is very active. It is undialysable, is precipitated by trichloracetic acid, and is inactivated by proteolytic enzymes. It differs from insulin in retaining most of its activity after incubation with alkali or with cysteine and in its much greater sensitivity to trypsin. It can be assayed by incubation with liver slices of well-fed animals when it very much increases the breakdown of glycogen to glucose. It acts in the same way as adrenaline, but the new preparation is twice as active per unit weight as adrenaline and has, apparently, a molecular activity at least fifty times that of adrenaline. Evidence points strongly to the production of glucagon by the α cells of the pancreatic islet tissue. Insulin is produced by the β cells. Glucagon has been extracted from the pancreas of a dog in which ligation of the pancreatic ducts had been followed by alloxanization three months later. Ligation destroys the acinar cells of the pancreas and alloxan destroys the β cells. Alpha cells can be damaged by treatment of the animal with cobalt chloride and there is considerable reduction of the glucagon content of the pancreas. While the evidence is not complete, it seems highly probable that glucagon is a hormone secreted by the pancreas. Significant differences are seen between dogs submitted to total pancreatectomy and those which have had either pituitary or alloxan diabetes. The depancreatized dogs suffer most severely of the three groups, though the dose of insulin needed to control the diabetes was lowest in the depancreatized dogs. Similar differences have been described between "true" diabetics and people who have become diabetic after pancreatectomy. Direct evidence that a glycogenolytic agent is secreted into the blood-stream by the pancreas of alloxanized animals has been demonstrated by cross circulation experiments. The only biological property of glucagon known with certainty is its ability to increase the rate of glycogenolysis in the liver. Unlike adrenaline, it has no effect on muscle glycogen, although its effect on liver glycogenolysis is very similar to that of adrenaline. On the other hand it does not influence the cardio-vascular system and does not increase the level of lactic acid in the blood as does adrenaline. The physiological defence against hypoglycæmia is essentially mediated by adrenaline acting directly on the glycogen of the tissues. On the other hand there is no evidence that glucagon discharge is caused by hypoglycæmia; rather, it seems, hyperglycæmia stimulates its secretion. It is possible that insulin and glucagon are secreted together during absorption of glucose from the gut causing the hepatic reserves of glycogen to be mobilized and stored in the periphery, thus preparing the liver for the uptake of newly absorbed glucose.

Much work is being done on the relations between insulin, glucagon and growth hormone, and there is evidence that all these substances are concerned with growth. Glucagon has become an important factor in all considerations of the ætiology of diabetes, and many of our concepts on the interrelationships between the endocrine glands will have to be revised in the light of the new knowledge which has accumulated.

[1] *Lancet*, July 18, 1953.

PROLONGED CORTISONE THERAPY IN RHEUMATOID ARTHRITIS.

SINCE 1949, when Kendall, Hench and their colleagues introduced cortisone as a therapeutic agent, much has been written about the short-term effects of this hormone and of ACTH. It is naturally taking longer to record and assess the effects of prolonged therapy, although the importance of this in relation to chronic diseases is obvious. A good deal of interest, therefore, attaches to the report of a study by Melvin H. Levin and five others,[1] carried out over a period of eighteen months, from September 1, 1950, to March 1, 1952. Information was sought on four points: first, the clinical effects and dosage requirements of ACTH and/or cortisone when used continuously for prolonged periods in patients with rheumatoid arthritis; second, the practicality of such continuous long-term treatment in the out-patient clinic, including the necessary clinical and laboratory follow-up; third, the comparative effectiveness of ACTH, parenterally administered cortisone, and orally administered cortisone; fourth, the nature and incidence of untoward effects from these drugs when given for long periods. Fifty patients with active rheumatoid arthritis were included in the study; 33 had rheumatoid arthritis of peripheral joints, 13 had combined rheumatoid spondylitis and peripheral arthritis, and four had rheumatoid spondylitis only. Their ages varied from twenty-three to sixty-one years with an average of forty-two years. The duration of the disease prior to therapy ranged from three months to twenty-five years, averaging 7·4 years. Throughout the course of hormone treatment, physical therapy and other adjunctive measures were continued. The total duration of therapy varied, but in 27 of the 50 cases, it was from nine to eighteen months. Three programmes of treatment were used: first, intramuscular injection of ACTH, followed by intramuscular injection of cortisone, followed by oral administration of cortisone; second, intramuscular injection of cortisone followed by oral administration of cortisone; third, oral administration of cortisone only. In all cases, initial "suppressive" therapy consisted of relatively high doses of hormone given in an effort to obtain rapid improvement; medication was then gradually reduced to an amount consistent with maintenance of most or all of the early benefit—that is, "maintenance" therapy. The early response to suppressive and maintenance therapy did not

[1] *Am. J. Med.*, March, 1953.

differ materially from that recorded by many investigators and need not detain us now. With long-term treatment, it was found that the degree of improvement was inversely proportional to the severity of the disease process, but the incidence of complete remission remained low even after prolonged therapy. Many patients, although not "cured" by the hormones, were greatly improved. Their tolerance to the disease was increased as indicated by their ability to return to work and live a happier, more productive life. Exacerbations of rheumatoid arthritis during therapy were not uncommon. To combat such exacerbations the precipitating factor was sought and controlled when possible, and in addition, the maintenance dose of cortisone was increased for varying short periods and the patient was readmitted to hospital when necessary. As a result, all minor recurrences promptly abated, as did some, but not all, of the major exacerbations. It is notable that gradual dosage reduction was less often followed by flare-ups than was sharp decrease in dosage. The observations on side effects are important. Levin and his colleagues report that 44 of the 50 patients had effects other than those to be regarded as beneficial. Of the six who had no evident side reactions, three were under treatment for only a very short time. In many cases, multiple side effects occurred. In 39 cases, one or more of the findings commonly ascribed to hyperfunction of the adrenal cortex developed, such as moon facies, hypertrichosis, weight gain, œdema, elevated blood pressure, sexual disturbance, personality changes and diabetes; in many cases, these conditions slowly decreased or disappeared with low dosage maintenance therapy, and œdema and hypertension were nearly always controlled with a diet of low sodium content and/or the administration of mercurial diuretics. There is nothing new or particularly disturbing about these side effects, but Levin and his colleagues are concerned about the appearance of other phenomena, some at least of which may be a direct result of ACTH or cortisone administration; these included the development of tuberculosis and other infections, *periarteritis nodosa*, renal disease, peptic ulcer and psychosis. The relation of the development of these conditions to the hormone therapy is still debatable, but Levin and his colleagues are by no means alone in reporting the occurrence of these major side effects, and it cannot be dismissed lightly. It should be noted that in 10 of their 50 cases, therapy was discontinued because of the seriousness of side effects, and four patients died. The experience reported here more than justifies a continued conservative approach. There seems to be no doubt about the beneficial effects produced, but the conclusion of these investigators should be heeded; it is that until more information is available concerning their hazardous propensities, it is probably inadvisable to employ these hormones for protracted periods in the treatment of arthritics, other than those who demonstrate progressive disease despite adequate trial of more conservative therapy.

TREATMENT OF BURNS.

DURING the past ten or fifteen years there has been a greatly changed emphasis in burn therapy. Earlier discussions were concerned with the types of dressings and local applications of drugs. At a conference on the treatment of burns held at Cornell University recently modern concepts of the treatment necessary after extensive burns in man were considered.[1] The principal speaker was J. Mulholland and the discussion was summarized by Dr. Ferguson. Within the first thirty-six to forty-two hours a burned area becomes œdematous, as a result of increased filtration from damaged capillaries. The œdema fluid contains electrolytes and significant amounts of protein which are then lost to the body economy. The amount of loss is related to the area and, to some extent, the depth of the burn. Half the extracellular fluid may be put out of use. Hæmoconcentration, vascular collapse, and kidney damage result. Therapy during the first forty-eight hours must correct these defects by administration of huge volumes of water, electrolytes (particularly sodium chloride or mixtures of this with sodium bicarbonate) and blood or plasma (or suitable substitutes). A convenient formula is: Administer in the first twenty-four hours one millilitre of blood or plasma for every kilogram of body weight for every percentile of surface area burned. Thus a 70 kilogram man, burned over 35% of his area, needs 2500 millilitres of osmotic fluid in the first day. A similar amount of physiological salt solution and an additional 2000 millilitres of water should be given also. In the second twenty-four-hour period one-half of these amounts is given. By the third day the dangers of œdema fluid collection and dehydration are generally well over and diuresis of the œdema fluid may be anticipated, so care must be taken at this stage not to overload the circulation. As blood and plasma are limited in availability, consideration should be given to substitutes, particularly dextran. If the patient survives, early skin grafting must be considered. This reduces surface loss of fluids, speeds recovery and reduces scar tissue. There is still considerable controversy about the local treatment of burns which should go on concurrently with the fluid treatment. Some advocate pressure dressings, but equally good results have been obtained by the use of no dressings whatever and the avoidance of any pressure even of the bed clothes. With ordinary aseptic precautions an uncovered wound remains clean and non-suppurating and gives little pain or discomfort. The open burn is soon covered by a dry, smooth, impermeable coagulum. There is still doubt about the value of ACTH and cortisone in treatment. Mulholland considers that this treatment should be reserved for those persons with a burn which would ordinarily be considered lethal. Various digestive enzymes have been tried to help in the early removal of the slough, but there is no unanimity as to the value of this treatment. Where the slough can be removed surgically it is a great advantage, but this does not often occur except in electrical burns.

[1] *New York State J. Med.*, April 15, 1953.

MARCH HÆMOGLOBINURIA.

HÆMOGLOBINURIA has been observed after exposure to cold and after heavy or unwonted exercise. Since military training his subjected young men not specially accustomed to hard exertion to various types of exertion of an unusual kind, a number of the studies have been made on young recruits. Hence comes the name "march hæmoglobinuria", though, like many arbitrary names of medical syndromes, it is certainly too dogmatic to be true. First described some seventy years ago, it was noted in Germany during the First World War, and appeared in the literature again during the 1939-1945 war. Lucy Bryce published an article on the subject in this journal in 1944.

B. H. Chaiken, E. J. Whalen, N. Learner and N. J. Smith have now drawn attention to variants of the usual form of the syndrome, and give details of studies which they have carried out on two patients.[1] Hitherto the carrying out of exercise in the erect posture and in particular the assumption of a lordotic posture have been suggested as of some ætiological importance, but these authors note that one of their patients was a young man who passed brownish-red urine after completing an exercise in the prone position, and dragging his body over and under various obstacles. The other young man, also an army trainee, had similar symptoms after doing a great deal of walking, standing and bending. The first subject had noticed two similar episodes before entering the army. In each of these he felt chilly, and suffered dull pain in the region of the costo-vertebral angles, but this, and the passage of brown urine, beginning some hours after the exercise, disappeared after a night's sleep. He had a further attack after swimming. His family history showed that his father had episodes of passing blood-stained urine as a child, but these disappeared after two years. The authors carried out an extensive series of investigations on the blood and its chemistry, and com-

[1] *Am. J. M. Sc.*, May, 1953.

pared some of the findings with observations made after exercise. The most interesting studies were those made with radioactive iron (Fe_{59}) administered by mouth. The radioactivity of the man's plasma was estimated before and after exercise, together with hæmatocrit readings and estimation of the plasma volume. The last-named test was made with the Evans-blue dye method, and it is admitted that errors may occur with this technique. In the first patient it was calculated that about 65 millilitres of whole blood or 29 millilitres of packed red cells were hæmolysed. About one-third of the released hæmoglobin appeared in the urine. The second patient was unusual in that hæmolysis was observed in specimens of blood, and a significant number of red cells were present in the urine. The first patient was submitted to most detailed investigations with the object of ascertaining whether the syndrome could be produced by exercise of various kinds carried out in different postures. Marching after the application of a lordotic cast to the body did not excite hæmoglobinuria, nor did the wearing of a kyphotic body cast prevent it. Investigations did not reveal abnormality of either kidney. In the second patient no cause for hæmaturia or hæmoglobinuria could be found, but there was no doubt that hæmoglobinæmia occurred unrelated to hæmolysis after the passage of urine. Therefore the authors have no hesitation in regarding both cases as illustrating variants of this syndrome. Certainly the trouble taken in the investigation of the first patient seems to establish that hæmoglobinuria appeared only after exercise in the horizontal posture, that it could not be demonstrated to be related to congestive factors in the renal vascular system, and that lumbar lordosis was in no way related to the appearance of blood pigments in the urine. The effect of ACTH was tried on the first patient; this was followed by a remission, and on the day following administration of the ACTH and thereafter for some seven months, the syndrome could not be reproduced by exertion. The authors are careful to state that no conclusions should be drawn from this one experience, but further trials would seem to be justified. Though "march hæmoglobinuria" appears to be rare, it is not impossible that it occurs under other circumstances, and its investigation should be pursued, for hæmoglobin still holds secrets.

THE HYPERVENTILATION SYNDROME.

THE classic sequel of hyperventilation is usually considered to be an episode characterized by muscular spasm which displays some degree of tetany. Of course hyperventilation as a physiological experiment, such as has been demonstrated in the earlier history of physiological medicine, no longer surprises even the most ingenuous of clinicians, but perhaps the varied nature of those usually "functional" attacks is not always suspected. Bernard I. Lewis goes farther than this, for he states in a recent communication that hyperventilation syndromes occur frequently, and may pursue a chronic course punctuated by acute episodes.[1] He lists an extensive series of manifestations, and remarks that when chronic symptoms occur, other symptoms rarely associated with hyperventilation appear and confuse the diagnosis. This list of symptoms includes neuro-vascular, muscular, respiratory, cardiac, gastro-intestinal, psychic and "general" symptoms. Lewis counters the obvious objection that the syndrome has usually a psychogenic ætiology by pointing out that similar phenomena and symptoms are encountered in disorders of the central nervous system, in certain toxic states, in high altitude flying, and in intense emotional reactions even in stable individuals. Nevertheless, he reminds us that alkalosis is really easily produced, as a single deep respiration will decrease the arterial carbon dioxide concentration by 5% to 7%, and the carbon dioxide tension by seven to sixteen millimetres of mercury. More convincing is the statement that in sustained over-breathing most of the carbon dioxide reduction is accomplished in the first thirty to sixty seconds. Those who have witnessed an attack from the beginning will have been struck with the short preliminaries in this curious pseudo-emergency. The author regards the cerebral phenomena as protective, since he believes that changes in awareness, related to the demonstrable electro-encephalographic changes, though only in the time sense, tend to reduce the hyperventilation and thus avoid the onset of tetany. He also mentions disordered breathing, such as sighing or yawning respiration. This has been mentioned before in these columns; the general verdict is that this type of breathing is due to nervous factors. That circulatory changes occur is readily understood; all the alterations in breathing produced by hyperventilation set the stage for vasomotor disturbances, and for such signs as tachycardia and extrasystoles. There is no need to pursue the whole gamut of signs and symptoms which have been attributed to over-breathing. Surely it is better to recognize those phenomena which are without doubt caused by the biochemical variations in the body as true manifestations of this syndrome, and the other less defined symptoms as side effects. There seems little if any doubt that there are persons who are prone to these manifestations, and so are also prone to such happenings. Doctors are accustomed to observe that the clinical picture is often clear without any necessity to list every divergence from a strict norm, to which few if any of us conform either in health or disease. Lewis cites the histories of several patients who illustrate certain aspects of the extended syndrome which he describes. One patient had undoubted attacks of hyperventilation tetany, for which morphine was given, but it does seem a little surprising that after some months of illness it was thought advisable to use drug therapy ("Paredrine") and binders to control what is described as moderate orthostatic hypotension. The true nature of the acute episodes of hypoventilation was proved in some patients by the physiological antidote of making them breathe in and out of a paper bag. The author remarks that the immediate termination of a most alarming attack by so speedy and simple a device is reassuring to the patient, and also gives the physician insight into his condition. Lewis has described conditions which may occur in persons subject to the over-breathing syndrome, but it is questionable if it is right to assign a causal relation to signs and symptoms which may be readily observed in persons who never show this curious sensitiveness to changes of a particular kind in their biochemical balance. But it is good to be reminded occasionally of a condition that one rarely sees, and of the simplicity with which it should be relieved. Readers of medical fiction may remember one instance in which the doctor hero cured an attack of psychogenic tetany by smacking the patient's face. It seems a pity that the fashionable shop in which this occurred did not produce a paper bag.

[1] *Ann. Int. Med.*, May, 1953.

HALF-PINT MEASURES AND MEASURING SPOONS.

THE Standards Association of Australia announces the issue for public critical review and comment of a draft Australian Standard Specification for half-pint measures and measuring spoons as Document 251. This standard has been prepared at the request of the Dietetic Association of New South Wales, with support from other interested organizations. Lack of uniformity in respect of such measures has in the past created a good deal of confusion, and the purpose of the standard is to assist housewives and professional workers in the dietetic field by specifying definite capacities for "cup", "tablespoon" and "teaspoon". The specified capacity at the mark "cup" on the half-pint measure is eight imperial fluid ounces, while the specified capacities of the tablespoon and teaspoon are a half fluid ounce and an eighth fluid ounce, respectively. The spoons are intended both for cookery purposes and for measuring medicines. Copies of the draft specification can be obtained from the Standards Association of Australia, Headquarters Office, Science House, 157 Gloucester Street, Sydney, and from branch offices in all capital cities of the Commonwealth and at Newcastle, New South Wales. Comments on the draft should be sent to the Association not later than September 30, 1953.

Abstracts from Medical Literature.

PATHOLOGY.

Mucin-secreting Tumours of the Skin.

B. LENNOX, A. G. E. PEARSE AND H. G. H. RICHARDS (*J. Path. & Bact.*, October, 1952) describe 11 skin tumours containing substantial amounts of mucin. Five of these were of mixed salivary pattern, one resembled a mucoid carcinoma of the breast, and five were, with varying degrees of certainty, recognizable as hidradenomata. Except for small amounts in occasional rodent ulcers (six out of 150), mucin was not seen in any other type of skin tumour. These findings are believed in themselves to provide strong evidence that the mixed salivary tumour of the skin is a hidradenoma with excessive production of mucin. The authors state that transitional changes seen in one hidradenoma appear to support this. Eighteen distinct forms of hyaluronidase-stable mucin were identified in nine tumours studied histochemically. As many as four kinds were seen in one tumour. A broad grouping into four classes was possible on histochemical grounds, and in each class the mucin was found in a definite site: (*a*) in cells and small ducts, (*b*) in large cysts, (*c*) in contact with the stroma, (*d*) in cartilaginous material. Except for the presence of this last class, no consistent difference was noted between the mixed salivary pattern tumours and the recognizable hidradenomata. It is argued that the histochemical findings are best explained by the occurrence of physical changes in highly labile mucins in response to environmental changes, and that the stromal peculiarities of mixed salivary tumours may all be explained on this basis.

Cytochemistry and Cytology of the Normal Anterior Hypophysis.

A. G. E. PEARSE (*J. Path. & Bact.*, October, 1952) states that with the application of the trichrome-periodic acid-Schiff method to the anterior lobe of the hypophysis a new terminology is necessitated. By the use of this method it is possible to demonstrate mucoprotein in one form or another in a variety of cells. All the basophile cells and those Mallory chromophobe cells which contain mucoprotein granules or vesicles have therefore been called mucoid cells. Comparison is made between Mallory's and the new method by means of Rasmussen-type differential cell counts on horizontal sections. The mucoid cells constantly exceed the Mallory basophile cells by between 12% and 25%. Comparison is also made by descriptive methods, and it is emphasized that, provided a mucoprotein fixative is used, no qualitative change occurs in granules stained by the trichrome-periodic acid-Schiff method as a result of immaturity, autolysis, fixation or differentiation. This constancy contrasts sharply with the tinctorial differences produced by these factors when other staining methods are used. The mucoid cells have been divided into eight types: maximal, intermediate, punctate, disperse, vesiculate, hyaline, Crooke-Russell, polar bigranulate. These types are described and illustrated, and their significance is discussed. A differential count of 500 to 1000 mucoid cells is made the basis for a rapid method of estimating the degree of activity or otherwise of the gland in respect of mucoprotein production. The method is referred to as the maximal-intermediate count from the names of the two principal cells. Cyclical changes which occur in the nuclei and cytoplasm of the mucoid cells are considered and presented in the form of a mucoid-cell cycle. The distribution of mucoid cells in the gland is discussed. The constancy of the pattern in horizontal sections, first pointed out by Rasmussen, is emphasized and its embryological basis demonstrated. Finally, the problem of which cells secrete hormones is reviewed in the light of the results of the trichrome-periodic acid-Schiff method. It is concluded that no hormones which are derived from carbohydrate-containing precursors or are themselves composed of mucoprotein can be produced by the acidophile cells. Follicle-stimulating hormone, luteinizing hormone and thyrotropic hormone are therefore necessarily produced by the mucoid cells.

Recovery and in-vivo Survival of Human Red Cells.

I. W. BROWN AND H. F. HARDIN (*Arch. Surg.*, March, 1953) have made a study of seven lots of red cells stored in glycerin solutions at −70° C. up to six and a quarter months, and of one lot of red cells stored at −15° C. for fifty days as to quantitative recovery after rewarming and removal of glycerin and quantitative in-vivo survival after transfusion. Over 90% of red cells were recovered after storage at −70° C. and approximately 64% of these cells survived normally after transfusion. Of one lot of red cells stored in glycerin at −15° C., 79% were recovered intact, and 47% of these recovered cells survived normally after transfusion. No immediate or delayed reactions were encountered when these stored cells were transfused. There was evidence from these experiments that a large portion of the abnormal post-transfusion loss of stored cells was due to the incomplete removal of glycerin from some of the cells before transfusion. Other possible methods for the more efficient removal of glycerin are discussed.

Mucopolysaccharides in Mucus-producing Tumours.

EDITH GRISHMAN (*Cancer*, July, 1952) reports histological examination of 16 mixed tumours of the parotid gland, five colloid carcinomata of the breast, six myxomata and three myxosarcomata for the nature of their mucopolysaccharides. Sylven's toluidine-blue stain, McManus's periodic acid-leucofuchsin method and hydrolysis with various hyaluronidase preparations were used. It was found that mixed tumours contained two types of mucus, an epithelial type in the glandular structures and a mesenchymal type in the myxomatous areas, characterized by different staining reactions. The histogenetic theories of mixed tumours are discussed in the light of these findings. The mucus of colloid carcinomata of the breast was found to be of epithelial nature; that of myxomata and myxosarcomata was of mesenchymal nature. The author states that while hydrolysis with bull testis hyaluronidase proved to be specific in the differentiation between epithelial and mesenchymal mucus, an attempt to analyse further the mesenchymal mucus in myxomata and myxosarcomata by the simultaneous use of bull testis and streptococcus hyaluronidase was not successful.

Response to Injury in Various Tissues.

G. R. CAMERON AND R. M. L. MEHROTRA (*J. Path. & Bact.*, January, 1953) state that when small areas of rat tissue are frozen for short intervals of time, the necrotic cells are removed and replaced by reparative tissue at very different rates according to the site of freezing. The skin of the ear, the liver, the spleen, the pancreas and the voluntary muscle are rapid in their response to freezing, the fatty omentum, the kidney and the testis slow. While the adrenal occupies an intermediate position. Implanting frozen liver into a new environment such as the omentum or testis of the same animal is followed by retarded repair compared with that encountered in the natural liver environment. Atrophic change in the testis experimentally induced by massive dosage with œstradiol or by the induction of cryptorchidism results in accelerated response to local freezing. Variation in response to tissue injury may thus be referred to either the injured cells or the cell environment, and it is suggested that this dual relationship represents a kind of pathological unit for which the term "field" is suitable.

Cortisone in the Early Stages of Inflammation and Repair.

R. LATTES, J. WALLACE BLUNT, JR., H. M. ROSE, R. A. JESSAR, DE G. VAILLANCOURT AND C. RAGAN (*Am. J. Path.*, January-February, 1953) present a report on features of the early tissue responses of injury in cortisone-treated animals. The depression and inhibition of the inflammatory and reparative phenomena following injury during treatment with cortisone or ACTH have been previously reported by the authors and by other workers. The present investigations have shown that this inhibitory effect is not immediate, but follows a lag of half a day to four days, during which the morphological changes of injured tissues in cortisone-treated animals are essentially identical with those observed in controls. The type of injurious stimulus, whether mechanical, chemical or viral, is of no special significance. In an attempt to explain the differences in the course of the inflammation, the authors suggest that mucopolysaccharides do not undergo the same chemical changes in cortisone-treated animals as in untreated controls, and that, as a result, the chemical factors favourable for the post-initial phases of reparative reaction are deficient.

The Normal Glomerulus.

J. F. RINEHART, M. G. FARQUHAR, HAW CHAN JUNG AND S. K. ABUL-HAJ (*Am. J. Path.*, January-February, 1953) have studied the structural detail of the normal glomerulus by new histochemical techniques and electron micrographs. The basement membrane is considered to be primarily a differentiated cytoplasmic product of the endothelial cells. The surfacing epithelial cells elaborate a cytoplasmic secretion with properties of a mucopolysaccharide or mucoprotein. This substance is attached at many points to the basement membrane and is thinly spread over its entire surface. Evidence derived

chiefly from electron micrographs is presented which indicates that the epithelial mucoid penetrates the endothelial basement membrane at regular intervals of approximately 0·12μ.

Congenital Fibro-elastosis of the Endocardium.

N. F. C. GOWING (*J. Path. & Bact.*, January, 1953) reports three cases of congenital fibro-elastosis of the endocardium. One of the patients developed thrombi on the endocardium, with resulting embolism and gangrene of both legs. Previous case reports are reviewed and the gross and microscopic pathology is described. The ætiology and pathogenesis of the lesions are discussed. Available evidence suggests that the lesion represents an abnormality of cardiac development. There is no evidence that either maternal or post-natal infection is causative, although intercurrent infection in a child often precipitates the cardiac decompensation. Reports of endocardial sclerosis in adults are briefly reviewed, and it is concluded that the adult and congenital cases represent different disease processes.

MORPHOLOGY.

Development of Motor and Sensory Neurons.

K. MOTTET (*J. Comp. Neurol.*, June, 1952) removed the somatopleur from 42 chick embryos at sixty to seventy hours' incubation and from five embryos after five days' incubation. Embryos were killed at daily intervals after from four to eleven days' incubation, sectioned and stained and the histological development of the spinal ganglia and posterior and anterior horns of the cord was studied. A reduction in the number of differentiating motor neuroblasts in the basal plate occurred as early as the latter part of three days' incubation. The author states that the first change in the indifferent cells as they begin to differentiate is an increase in the volume of cytoplasm, the axon process extending toward the periphery, followed by further increase in the volume of cytoplasm and the development of dendrites. The number of cells present in the spinal ganglia, sensory horn and motor horn greatly exceeds the number of those that differentiate into motor neurons. Degenerating neurons do not occur in the embryos from which a limb-bud has been removed at sixty to seventy hours of incubation. Regressive changes are observed in the motor horn and spinal ganglia of those embryos from which a limb has been removed after five days' incubation. A reduction in the number of motor neurons is not observed unless the periphery removed is sufficient to interfere with the growth peripheralward of the nerve fibres. It was concluded from the foregoing observations that the regulation of the number of motor neurons in the spinal cord in chick embryos is achieved by the selective induction of the indifferent cells to differentiate. The same mechanisms that regulate the neuron number in the motor horn are also operative in the spinal ganglia. The results obtained are in full accord with Barron's hypothesis and observations explaining the mechanism of induction. The results do, in fact, demonstrate that the mechanism is applicable not only to the cells of the motor horn, but to the spinal ganglia and sensory horn cells as well.

Properties of Compact Bone.

W. T. DEMPSTER AND R. T. LIDDICOAT (*Am. J. Anat.*, November, 1952) examined test samples of human bone to determine certain properties and how they varied in different axes. Compact bone was shown to be non-isotropic; in other words, it did not have the same physical properties in every direction. The findings are discussed in relation to data in the literature and to their significance in determining the effective and weak features of bone. The authors state that the study of bone failure and the correlation with the properties of bony material are still somewhat incomplete in accounting for why bones break as they do under excessive impacts and loading, in spite of the attention of numerous recent investigators.

Neurological Studies of the Cardiac Ventricles of Mammals.

F. DAVIES, E. T. B. FRANCIS AND T. S. KING (*J. Anat.*, April, 1952) state that only in Cetacea and Artiodactyla, among representatives of a large number of orders of mammals, did they find nerve cells to be numerous and extensive in distribution in the ventricles of the heart. This resemblance between these two orders is adduced as further support for their close systematic relationship. Unipolar, bipolar and multipolar cells were found in all the hearts. From the morphological appearances and the presence or absence of nerve endings in relation to the cells it is suggested that the multipolar cells may be efferent and the unipolar and bipolar cells afferent in function. Only simple nerve endings were found related to the various tissues comprising the ventricles. It is suggested that the spiral nerve endings around ventricular myocardial fibres are sensory stretch receptors, and that the simple nerve endings in the adventitia of the coronary arteries may be concerned with the cardiac pain mechanism. In the present work the nerves accompanying the auriculo-ventricular bundle and its limbs were found to be relatively few in number, except in Artiodactyla and Cetacea. Many of them were noted to leave the bundle in the early part of its course to pass into the myocardium of the ventricular septum, but it appears to the authors that these nerves are far too few to contribute materially to the plexus of nerves in the septum, the latter being mainly derived from the epicardial nerves. This observation, coupled with the failure to find any motor nerve endings in the myocardium, leads to doubt as to whether the nerves accompanying the bundle can be concerned with the conduction of the impulse from atria to ventricles. Further, if these nerves did convey the impulse to the septal musculature, it might be expected that the upper part of the septum would be activated first, since the earliest nerves to leave the bundle enter this part of the septum, and that the process of activation would extend downwards through the septum. However, the extensive investigations in dogs by Sodi-Pallares *et alii* (1951) show that activation of the ventricular septum is from below upwards, and that the times of arrival of the waves of activation at different points on the right and left surfaces of the septum are in conformity with the distribution of the branches of the two limbs of the bundle. In the present work it was found that the bundle in the dog contains relatively few nerves, and that many of these leave the bundle to pass into the upper part of the septum, while the limbs of the bundle contain no nerves at all. It is submitted that these observations, considered in conjunction with those of Sodi-Pallares *et alii*, are strongly in favour of the conduction of the impulse from atria to ventricles by the auriculo-ventricular bundle and its limbs.

Reinnervation of Striated Muscle after Acute Ischæmia.

D. B. ALLBROOK AND J. T. AITKEN (*J. Anat.*, October, 1951) studied the histological changes which took place in a muscle after partial devascularization. They state that if the damage to nerve and muscle is slight, recovery follows without disorganization. When the terminal parts of the motor axons are involved, regeneration results in a number of fine axons growing down the old neurilemmal tubes, and groups of single atypical end-plates are formed. Extensive damage and necrosis are followed by regeneration of both muscle and nerve; details of this process are described by the authors. They state that end-plates are not visible until after about twenty-one days, and after twenty-eight days many of them are well organized. The pattern of innervation, however, remains very atypical, and it is not known whether further recovery occurs, owing to the development of fibrous tissue between the muscle fibres.

Developmental Formation of Muscle Architecture.

K. W. JAGER AND J. MOLL (*J. Anat.*, October, 1951) studied the development of the human calf muscles (*triceps suræ*) in embryos, stillborn fœtuses and adults. Special attention was paid to the development of muscle architecture and skeletal attachments. The author states that the *triceps suræ* arises from an independent rudiment, and a remarkable shifting of the muscle occurs during development. In the youngest stages it has a lateral position, the final position being reached only gradually. The medial head of the gastrocnemius is formed after the lateral one, but a migratory process does not occur in the formation of the medial head. Originally the heads of the gastrocnemius are attached to the skeleton in an area of considerable extent. In later stages these primitive origins become concentrated into the much smaller final skeletal attachment. The soleus shows a marked extension towards the medial side of the leg. The tibial origin develops much later than the fibular. In early development the soleus originates diffusely from an area of great size. The characteristic muscle architecture of the soleus and gastrocnemius is obtained by considerable rearrangement of the fibres and by their increase in number. These arrangements take place in connexion with a transformation of the tendons, originally rather small, into large aponeuroses.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

LXXVII.

DRIVING UNDER THE INFLUENCE OF INTOXICATING DRINK.

BILL is an ordinary chap of forty years of age and weighs 11 stone, he is accustomed to a few drinks and is an average driver. He went to his club at 6 p.m. and had a few whiskies (one whisky equals one ounce of 40% alcohol); he left at 7 p.m., picked you up at your rooms at 7.10 p.m. and drove you home. As he turned into your street your wife, with two children hanging onto her dress and she pushing a pram with her baby, is just about to cross the street! What is the maximum number of whiskies you would have allowed Bill if you could have anticipated the event?

This question was put to 150 medical men representing a fair cross-section of considered medical opinion. The results were as follows:

Two would not give an opinion; three from lack of experience had no idea	3%
Seven said none	5%
Sixteen said one	11%
Seventy-six said two	51%
Twenty-six said three	17%
Eighteen said four	12%
Two said five	1%

This means that 66% said two whiskies or less and 84% said three or less.

Under the conditions of the experiment, with concentrated alcohol on an empty stomach and allowing approximately one and a half hours for absorption, it is reasonable to assume that most of the alcohol was absorbed and still present in the blood and tissues. Knowing the weight of the man and the amount of alcohol in a whisky, we can calculate on the basis of three whiskies that the blood alcohol level was in the vicinity of 35 to 40 milligrammes *per centum*. Considering that among those who said four whiskies there were several big men and as in general the answer given was in terms of the amount of alcohol the individual doctor had found to affect his driving, one can confidently say that nine out of ten doctors have found from personal experience that a concentration of 40 milligrammes *per centum* of alcohol in the blood is sufficient to affect their driving—they are "under the influence".

It also stresses another point: namely, that the so-called great difference in toleration of alcohol is more apparent than real. No one would be so foolish as to deny that alcohol affects different people differently and has a different effect on individuals under different conditions, but when we ignore differences in psychic behaviour and confine our attention to the four cardinal requisites for safe driving—attentiveness, alertness, coordination and responsiveness—the differences in individual tolerance are greatly reduced. Says the sceptic: "Harry has a couple of drinks and becomes garrulous, laughs at the top of his voice and wants to kiss everybody, while Tom can sink half a dozen stiff whiskies without turning a hair; alcohol affects everybody differently; with so much individual variation it's absurd to place reliance on blood alcohols." The party is over, Harry gets into his motor car and drives safely home—he may have had a few inhibitions removed, but his four cardinals are unimpaired. Tom gets behind the wheel and backs his motor car straight into the one behind—and his wife drives home! The level of the blood alcohol would tell a very different picture from their outward behaviour. Harry's blood alcohol after his couple of drinks would be far below 40 milligrammes *per centum*, while Tom's would be in the hundreds.

A great deal of controlled research has been done on the correlation between blood alcohol levels and the effect different concentrations have in different individuals; the more carefully the work has been done, the smaller the range of tolerance. In other words the great majority of individuals show impaired cerebration at approximately the same level of blood alcohol. This will be discussed in more detail later.

Factors which Influence the Blood Alcohol Content.

Concentration of Alcohol.—When alcohol is drunk it is contained in the stomach and for a time some rapidly diffuses through the mucosa, but owing to an outpouring of gastric juice the percentage of alcohol is soon reduced to between 3% and 4% and absorption from the stomach slows down. The alcohol passing into the intestine is rapidly and completely absorbed. The more concentrated the alcohol, the more rapidly it is absorbed. Cocktails and fortified wines—20% alcohol—are among the most concentrated forms of alcohol consumed; whisky and other spirits are generally broken down from their 40% to below 20% by the addition of other fluids. Beers vary between 4% and 5%. One would find that with a given quantity of alcohol taken on an empty stomach the blood alcohol content would rise most quickly and go to the highest level in those who had cocktails and sherry, next with the spirit drinkers, and most slowly and at the lowest level with those who "played safe" and drank beer. How often do we hear the remark "that sherry went straight to my head".

Food.—The presence of food and fluid in the stomach greatly slows the rate of absorption, partly by dilution, partly by retaining the alcohol in the stomach. Carbohydrate, meat and milk are found to slow absorption more than fat. Alcohol is not metabolised in the stomach or intestines and none is excreted in the fæces. All the alcohol ingested and retained is completely absorbed unchanged.

The Fate of Absorbed Alcohol.

Once in the veins of the alimentary tract, the alcohol passes to the liver, where oxidation begins; the concentration of alcohol is greatest in the portal veins. The alcohol in the hepatic veins passes to the heart and is there diluted with blood from the rest of the body. In the lungs some small amount diffuses into the alveolar spaces and this gives the "smell of alcohol" to the breath. Returning to the left side of the heart, the alcohol passes to the capillaries and diffuses out into the water of the cells and interstitial spaces till equilibrium is established between the concentration of alcohol in the water throughout the body. This equilibrium is maintained during the whole of absorption and subsequent metabolism of the alcohol. The characteristic effects of alcohol are determined by the concentration of alcohol in the water of the brain cells.

The Metabolism and Excretion of Alcohol.

Oxidation.—By far the greatest amount of alcohol is removed by oxidation and the liver is the most important organ. It is generally agreed that the energy produced is available, so that alcohol is a food. Oxidation is a slow continuous process; the rate is an individual variant, but is of the order of one-third of an ounce (10 millilitres) per hour. This is equivalent to about three-quarters of a standard whisky or three-quarters of a "middy" of beer—a "middy" is half a pint. Alcohol is so diffusible that it is present in any fluid lost by the body. In the urine it is somewhat more concentrated than in the blood. The amount lost in the urine, sweat and expired air obviously varies according to circumstances, but the range is comparatively small—from 1% to 10% of the amount absorbed.

Quantitative Aspects of Absorbed Alcohol.

The average weight of a man is 70 kilograms (11 stone), and though there is considerable variation in water content from one individual to another, and in the same individual at different times, one can say on a fair average that the human organism is 70% water. The blood, also subject to variation, weighs in an average man 12·5 pounds and is 85% water, so that an average man weighs 154 pounds and has 109 pounds of water of which 10·6 pounds are in the blood. The blood water is approximately one-tenth of the total water. There is always equilibrium in the concentration of alcohol throughout the water of the body, so that there is always nine times as much alcohol in the water of the tissues and tissue spaces as in the blood. With these data an approximate calculation can be made of the amount of alcohol that has been absorbed at any given level of blood alcohol.

Let us assume a blood alcohol level of 100 milligrammes *per centum*. One hundred millilitres of blood contain 0·1 gramme of alcohol; 100 millilitres of blood weigh approximately 104 grammes, and in 12·5 pounds (weight of blood) there are 5700 grammes. Therefore the total amount of alcohol in the blood will be $\frac{5700}{104} \times 0{\cdot}1 = 5{\cdot}4$ grammes and the total amount in the body will be 10 times this amount = 54 grammes. Fifty-four grammes of alcohol equal 70 millilitres approximately (1·0 gramme alcohol = 1·27 millilitres). Seventy millilitres of absolute alcohol are contained in some six whiskies or six "middies" of beer.

In short, 0·1 gramme *per centum* of alcohol in the blood in a man of 11 stone means that the equivalent of six whiskies or six "middies" of beer has been absorbed. The amount consumed would always be greater because not all the alcohol is absorbed at once or at one time and the

metabolism and excretion of the alcohol already absorbed are already proceeding.

Validity of Using the Blood Alcohol Level as Evidence of Degrees of Intoxication.

It can be seen, therefore, that, even allowing for a considerable range of variation in the various factors determining it, the blood alcohol level provides, with sufficient accuracy for the purpose, scientific and factual proof of the quantity of alcohol absorbed.

As there is no doubt that the level of the blood alcohol is determined by the amount of alcohol absorbed after consumption and no doubt that it is the alcohol absorbed that exerts its effect on the brain, we have only to correlate blood alcohol levels with experimental evidence of impaired function to test the validity of the use of blood alcohol levels in law. Apart from the innumerable observations of every intelligent person who consumes alcohol and who watches the effect of the consumption on others, there has been an enormous amount of controlled experimental work in various parts of the world, mostly in Scandinavian countries, in Great Britain, Canada and the United States of America. Firstly, it is obvious that if a person has no alcohol or only a low concentration, the person is not "under the influence". This in itself could be, and in actual cases has been, most important. Instances of brain injury, shock, hypoglycæmia, illness *et cetera* giving rise to signs and symptoms suggestive of intoxication are on record. Leaving out for the time being the question of toleration or habituation, we can say that there is world unanimity that at a level of blood alcohol between 30 and 40 milligrammes *per centum* the vast majority of individuals, including those accustomed to take alcohol regularly, can be shown by a large variety of tests, including driving tests, to have mental impairment of such a degree as to be legally and medically "under the influence". This range of figures was stressed again and again in the Proceedings of the First International Congress on Alcohol and Traffic. It is therefore no coincidence that the opinion expressed by the medical men in Sydney was in accord with the findings in other parts of the world. Bjerver and Goldberg, of the Pharmacological Department, Karolinska Institute, Sweden, concluded their paper with the significant sentence: "The threshold of impairment of driving ability in expert drivers accustomed to consuming moderate amounts of alcohol is an alcohol concentration of 0·035 to 0·040 per cent in the blood."

The findings of Professor H. Ward-Smith, of the Department of Pharmacology, University of Toronto, are likewise confirmatory. His conclusions were based on a survey of the alcohol content of the blood of drivers concerned in traffic accidents.

The figure accepted as *prima facie* evidence of being "under the influence" varies considerably in different countries. In Norway it is 0·05 gramme *per centum*, while in the neighbouring Sweden it is 0·08 gramme *per centum*. In Switzerland a figure of 0·100 gramme *per centum* is used as a limit figure, but it is not legally defined, though it is recognized there as "a very high figure". In the State of New York and many other States of America the law recognizes a range of figures. Below 0·05 gramme *per centum* is *prima facie* evidence of sobriety, from 0·05 to 0·15 gramme *per centum* is relevant evidence but not *prima facie* evidence; above 0·15 gramme *per centum* is *prima facie* evidence that the person is "under the influence".

Having followed the evolution of the significance attached by courts of law to blood alcohol concentration, one appreciates that years ago when "driving under the influence" was relatively of minor importance, the legal levels were fixed to coincide with the clinical condition of drunkenness, but with the rapid growth of traffic and of deaths and accidents on the road, it has become obvious that the dangerous person is not the drunken driver but the drinking driver, and there is a general tendency to fix the legal level at a figure where judgement begins to be impaired.

From all the evidence available it would appear that the acceptance of a figure of 0·05 gramme *per centum* of blood alcohol above which it would be *prima facie* evidence of being under the influence would be fair to the vast majority of drivers. Those who may raise the bogey of unfairness to the exceptional person and to the habitual drinker, beg the question. Before a person is taken into custody, his behaviour must have excited the attention of the constable or there must have been an accident. If the arrest is made on the first score there will be evidence apart from the level of the blood alcohol, and if an accident has occurred there will in general be plenty of evidence for and/or against those involved. Under all conditions the blood alcohol level is at most only one part of the evidence.

The Question of Tolerance or Habituation.

There is no doubt that, as it can to all other pharmacological substances, the body accustoms itself to alcohol on repeated exhibition; but the degree of tolerance is by and large not appreciable. Goldberg after prolonged experiments on this subject concluded that the heavy drinkers do have an increased tolerance, but the extent is only of the order of 0·04 gramme *per centum* of blood alcohol; in other words even an habitual heavy drinker shows definite impairment at alcohol concentrations of from 0·07 gramme to 0·08 gramme *per centum*.

How Does Alcohol Affect the Ability to Drive a Motor-Car?

It is generally admitted that alcohol in all doses acts as a depressant to the nervous system and that the apparent stimulating effect is due to the removal of inhibition of the higher centres.

Over-Confidence.—Many people claim that they can drive better after the ingestion of alcohol, but controlled experiments on such people show that this is a false confidence and that their actual performance is impaired. This very confidence is therefore a source of danger.

While conducting the survey mentioned in the opening paragraph, I got into holts with a medical man at a party. He eloquently discoursed on the rights of man in a free country and said that there was no law against having a drink. "Look at me", he exclaimed, "I had six whiskies before coming here and I am as sober as a judge." Later on in the evening his wife drew me aside and said: "I did my damnedest to make him let me drive here."

Psychic Disturbances.—Under this heading one can group changes in behaviour peculiar to the individual which are so commonly used to reinforce arguments as to the different degrees in which alcohol affects people; but psychic disturbances must not be confused with factors affecting the four cardinals—attentiveness, alertness, coordination and responsiveness. Some psychic disturbances are important in themselves as sources of danger—the tendency to "show off"; the urge to beat the yellow light; the determination not to let another car pass; the insistence on the right of the road, and the host of other discourtesies so apt to be manifested by drivers after they have had a few drinks.

Disturbances Affecting Eyesight and Reaction Time.—It has been adequately proved that comparatively small doses of alcohol are sufficient to restrict the fields of vision—the channel driving or tunnel driving phenomenon. In short, alcohol does to the driver what blinkers do to the horse, the only difference being that a driver who is oblivious to vehicles and pedestrians approaching from the side has no one at the reins to pull him out of trouble.

Reaction Time.—Alcohol definitely slows reaction time so that a stimulus reaching the eye is not conveyed as rapidly as normally to the motor centres and the motor response is also delayed. The degree of impairment in reaction time need obviously be only very small under modern driving conditions to determine the difference between a collision and a safe passage.

Disturbances Affecting Powers of Concentration.—There can be little argument that few if any human activities require such consistent and prolonged concentration as driving a motor-car. How often does one hear the remark: "You can't take your eyes off the road for a single second." There is no need to stress to anyone who has attended a lecture after a good dinner the point that alcohol does affect concentration.

Disturbances Affecting Judgement of Distance and Time.—These are also too commonplace to labour, yet both require only small quantities of alcohol to be affected.

Disturbances of Coordination.—Though the number of different processes that have to be coordinated in driving are relatively few, their timing has to be rapid and exact, and it has been adequately proved experimentally that coordination is affected by quite a low concentration of alcohol in the blood.

The Clinical Examination for Determining Whether a Person is "Under the Influence".

Perhaps there is no greater anachronism in medico-legal practice than the clinical examination used to determine for purposes of court evidence whether a person is "under the influence". It is generally agreed that in the vast majority of persons the ability to drive safely begins to be impaired at blood alcohol concentration of some 40 milligrammes *per centum*, but to prove this impairment the clinician uses yard-sticks which may not become apparent below a blood

alcohol concentration of 150 to 200 milligrammes *per centum* —"glassy eyes", "incoherent speech", "staggering gait", "disarranged dress" *et cetera*. Anyone giving thought to the problem must admit, after considering modern transport, with the high roads full of powerful lethal weapons hurtling along at 30 to 50 miles per hour in two or more directions at once, and streams of pedestrians of all ages and agility attempting precarious passages through intermittent interstices in the masses of projectiles, that such yard-sticks are no longer germane to the problem.

Quite apart from physical signs *per se* we have to take cognizance of the observer as well as of the observed. Thus Professor Liljestrand showed "the inconsistency of clinical examination and the wide variation between different examiners" as to diagnosis of "under the influence" by studying 700 reports from seven different physicians. As one example it may be mentioned that one examiner gave his verdict of "under the influence" in 43% of the cases with a blood alcohol concentration of 0·1% to 0·15%, while another made the same decision in 91%. When one or the other symptom was studied, the discrepancy was still more obvious. At 0·15% to 0·20% one observer stated that 6·0% of his subjects showed a "slow pupil reaction" against 83% observed by another, a positive Romberg sign in 27% against 100%, or a positive finger-finger test in no case against 81% observed by another examiner.

Professor Ornulf Odegard stated:

> The Oslo material seems to indicate that even experienced police psychiatrists will gradually improve their clinical diagnosis. In 1930-35 Dr. Lofthus reports 315 persons with a blood alcohol content of above 0·15, and of these he found 41 to be sober on clinical examination. In 1936-39 he found only 7 out of 207 similar cases to be sober, and in 1939-45 only one single case out of 200.

Safe Margins of Expert Drivers.

One aspect that has often been raised is that some drivers are so expert that they are still safer than other drivers even though they are under the influence. The fallacy here is: (i) The 100% efficient drivers are responsible for avoiding numerous accidents which less efficient drivers would not have avoided. (ii) If marked discrepancies exist between the efficiency of drivers then the requirements for obtaining a licence are too lax. (iii) Most important, there is no excuse under modern traffic conditions for anyone to drive with less than their total efficiency and so be more prone to accidents.

The Medical Attitude to the Introduction of Compulsory Blood Tests.

Whether compulsory legislation is to be introduced or not is a question for the elected representatives of the people, but once it was introduced the medical profession would naturally cooperate with the authorities to ensure the smooth running of the law. As a profession we are not concerned with punishment, but with the prevention of accidents and deaths, and we recognize that the chief purpose of compulsory blood alcohol tests would be to draw attention to the blood alcohol level which begins to impair a person's driving ability, and by propaganda to translate this into the amounts of alcohol that can be safely imbibed. Such legislation would be part of a comprehensive educational campaign to inhibit people from driving while under the influence.

More and more countries are introducing such legislation, and reports from all countries where the law has already been in operation—for example, Norway, Sweden and Denmark *et cetera*—are favourable.

It may rightly be asked if traffic accidents in Australia are of such a magnitude as to warrant more safety measures than are at present in force. The survey of The Danish Committee for Road Safety, "World's City Traffic", for the years 1950-1951 (the latest available) details various statistics concerning traffic for 49 of the world's largest cities. The average death rate from traffic accidents per 100,000 of the population for the year 1951 was 9·13. Of the 49 cities listed, Melbourne had the highest rate (22·41) and Sydney (including the whole of New South Wales) came next with 21·67! (No other Australian cities were listed.) The only near rival we have for killing people on the road is Johannesburg with 19·54.

Need the question whether the medical profession should support more stringent safety measures be further debated?

A Few Notes on How to Drink.

May I conclude with a few notes on how to drink?

1. The more dilute the beverage, the slower the absorption and the lower the ultimate blood alcohol level.

2. The more spaced the drinks, the more time is allowed for the alcohol already absorbed to be oxidized or excreted.

3. The longer the time since the last drink and the time of driving, the lower the blood alcohol will be. The "one for the road" is definitely out!

F. S. HANSMAN,
Sydney.

LXXVIII.
"DRIVING UNDER THE INFLUENCE": SOME LEGAL ASPECTS OF THE PROBLEM.

HAVING considered the medical side of the problem, let us now turn to the legal side, but before doing so it may be as well to remember that, although it is the duty of the Court to hear the evidence of experts, the Court can never dispense with its obligation to form an independent opinion (Richmond *v.* Richmond. 111. L.T. 273) and it is equally obvious a Court cannot do this unless it weighs all the evidence, including the opinion of experts.

Like the medical profession, the Legislature has not kept pace with the many problems the motor vehicle has caused. In Courts of Law, when faced with the drinking driver, we, like the medical profession, still have to rely on the same tests which have grown out of human experience with drunken persons and not individuals in a less than totally inebriated state. We still make a fetish of the expert; yet, provided there is no medical cause for a person's condition, the ordinary man in the street is just as competent as the expert to give an opinion on the presence of gross insobriety. Whether a person is in fact intoxicated is usually determined by noting his ability to walk or stand; his speech; odour of his breath; colour of face; the tremor of his hands; the condition of his eyes; and any other unusual act which deviates from the accepted norm.

The value of this method is further weakened because it is not the "drunk" who is the real traffic hazard, but the driver who is moderately influenced so that he is deprived of that clearness of intellect and control which is so necessary in these days of traffic congestion. The effects of alcohol are such that some drivers who have really succumbed to the influence of the liquor they have consumed can appear quite sober, especially when confronted with a person in authority. It is disconcerting to hear some doctors disagree with this proposition, while others vouch for its correctness. The consensus of authoritative opinion is that an accident or the shock of arrest can sober a person up. Let me illustrate. B was charged with driving "under the influence". There had been an accident and he had been taken to the doctor's surgery for treatment for a cut in his arm. He was most insulting and abusive to the doctor. About twenty minutes later the police arrived. The doctor informed them that, in his opinion, B was well "under the influence". However, when the police entered, B quietened down, but in view of the doctor's opinion they arrested him. In cross-examination the police officers admitted that it was only owing to the doctor's diagnosis that they charged the defendant—they would not have been satisfied by what they themselves saw to warrant arresting B.

C, a young man of good family, was involved in an accident and was later charged with causing grievous bodily harm by a negligent act (driving under the influence). Evidence for the prosecution tended to show excessive speed, but the only abnormalities the police and private witnesses noted were hesitant speech, flushed face, odour of liquor, watery or glassy eyes and confusion as to direction. These symptoms could have been caused by means other than the ingestion of alcohol. However, a blood test showed a blood alcohol level of 0·146%. The blood test was taken three hours after the accident and was not analysed for more than forty-eight hours after it was taken, so it is fair to assume that the blood alcohol level at the time of the accident was between 0·15% and 0·20%. C was nineteen years of age and not a seasoned drinker.

On the other hand it is quite true that some persons "go to pieces" under similar conditions, and the "crying drunk" is not uncommon.

It is against this background we consider the term "under the influence". Now one of the elementary legal rules of construction is that words must be given their ordinary grammatical meaning unless the context otherwise requires. The ordinary meaning of "influence" is to sway, to bias, or the ability or power sufficient to produce some effect. To be under the influence of intoxicating liquor a person has to imbibe sufficient liquor to produce some effect. He must be swayed or biased by the liquor he has consumed. The term, therefore, denotes a comparison between a person's behaviour after having consumed liquor and the normal person in full

command of his faculties. The question of drunkenness does not enter into the picture at all. Although all persons intoxicated by the consumption of alcohol are under the influence of such liquor, the reverse is not necessarily true, for a person may be in some degree under the influence without in fact being intoxicated.

It has been proved that even a small amount of liquor has some slight effect on the normal person, but "drinking" of itself is not an offence; if it were, then the Legislature would have to prohibit driving after a person had consumed any intoxicating liquor. There are, of course, some individuals whose behaviour is affected even by one small glass of liquor, and these persons come within the decision of the late Sir John Bavin in Molloy *v.* McDonald (56 W.N. (N.S.W.) 159) "who might be rightly described as under the influence". Let me again illustrate. B, a young man aged twenty-two years, came from a highly respected family. At about this time he decided he would have an occasional glass of beer. The result was disastrous; he became quarrelsome, he assaulted his mother and father and at different times committed other offences, during all of which he displayed signs of intoxication. Things reached such a stage that prison seemed the only alternative, but the Court was struck with his repeated assertions that he had only one, or, at the most, two glasses of beer before he committed these offences. Medical evidence established that he was highly "sensitive" to alcohol.

The decision in Molloy *v.* McDonald, previously referred to, prevents a Court reading into the offence the test whether or not the individual is capable of driving. The tests of drunkenness, the quantity of liquor consumed, and the apparent ability to drive must be discarded. It will be agreed that driving a motor vehicle involves a succession of highly skilled muscular movements dependent on rapid coordination of eyes, hands and feet. The drinking driver may to all intents and purposes appear to be driving efficiently, but place him in a position where he must exercise a choice or a series of rapid movements to avoid an accident, then he may become a traffic hazard. Let us assume that this driver sees a child dart from the kerb. The seeing acts as a stimulus and produces a response—you push down the brake and clutch pedals in order to avoid running the child down. The entire process of perceiving the dangerous situation, the nerve impulse transmitted to the brain, the brain telegraphing the nerves of the legs to stop the car, and the response of the legs to bring the requisite pressure on the pedals, all take a definite length of time. If this reaction time is slowed by half a second—at 30 miles per hour a car travels approximately twenty-two and a half feet (speed *plus* half equals approximate feet travelled per second)—this extra distance travelled may have meant all the difference between the safety of the child on the one hand or its injury or death on the other.

Very few definitions have been given by the various Courts as to what constitutes "under the influence". In Queensland it was held sufficient for the prosecution to prove that "as a result of the consumption of liquor the mental or physical faculties of the accused are so affected as to be no longer in a normal condition" (Noonan *v.* Elsen (1950) Q.S.R. 215). In England the then Lord Chief Justice, Lord Coleridge, interpreted the phrase in connexion with an insurance policy and said it meant "under such influence as to disturb the quiet and equable exercise of the intellectual faculties of the man who has taken liquor, or under such influence as disturbs the balance of a man's mind" (Mair *v.* Railway Passengers Assurance Company Limited. 37 L.T. 356). Without sufficiently sensitive tests which can measure this deterioration, these decisions do not show us how we can ascertain whether the balance of a man's mind has been disturbed unless we can perceive clear objective symptoms.

The most comprehensive definition comes from Arizona, United States of America, where the Court said:

> The expression ... "under the influence" covers not only all the well known and easily recognised conditions and degrees of intoxication, but any abnormal mental or physical condition which is the result of indulging in any degree in intoxicating liquors, and which tends to deprive him of that clearness of intellect and control of himself which he would otherwise possess. If the "ability" of the driver of an automobile has been lessened in the slightest degree by the use of intoxicating liquor, then the driver is deemed to be under the influence of intoxicating liquor. The mere fact that the driver has taken a drink does not place him under the ban of the Statute unless such drink has some influence upon him, lessening in some degree his "ability" to handle the said automobile (Steffani *v.* The State (42 Pac (2nd) 615).

It will be noted that this definition establishes three conditions where a driver can be said to be "under the influence", and it is a complete one in both the legal and medical senses. These circumstances are:

(i) All the well-known and easily recognized symptoms of intoxication.

(ii) Any abnormal mental or physical condition as a result of imbibing intoxicating liquor.

(iii) Any lessening of a driver's "ability" in the slightest degree by the use of such liquor. ("Ability" as used here is not used in the sense of capacity to drive but in the sense of mental and physical ability.)

The tests of drunkenness, the amount of liquor consumed, and the ability of the driver to control his vehicle are discarded. The definition is in line with the report of the 1927 Special Committee of the British Medical Association (England) under the heading "Tests for Drunkenness". This committee pointed out that "finer shades of self control may be lost without apparent signs of intoxication"; and again in 1935 a similar special committee reported: "alcohol in an amount less than is customarily regarded as sufficient to render a person under the influence of alcohol to such an extent as to be incapable of having proper control, has definite effects on the human body".

Stages of Intoxication.

Most medical writers adopt four stages when dealing with intoxication, and it may be of advantage to apply the Arizona definition to these stages. For the purpose of this analysis the person who is "sensitive" to alcohol is disregarded.

The First Stage.

At this stage there may be a flushing of the skin, but the symptoms of excitement are not greatly in evidence unless the individual is subject to outside stimulus, such as social activities. In this latter case self-restraint is relaxed, and there is freedom of emotional response. The drinker converses well, laughs and smiles more readily, and, in some cases, becomes angry more easily. The will-power is not greatly affected; hence at this stage the drinker can reassert his self-control should the occasion demand. All of us have had the experience of attending a formal dinner party. The host welcomes us; most of the guests have not met before. The talk is formal and voices are low and restrained. Cocktails are produced. We toy with the first drink and then a second and third round are poured. The party "peps up" and soon men are calling each other by their Christian names, conversation flows freely and subject matters become less formal. As time goes on and more drinks are consumed, the tone of voice becomes louder and more boisterous and drinks are downed with a gulp. Inhibitions are thrown aside, and at the end of the evening everybody departs feeling exhilarated.

This result is brought about because one of the first results of imbibing alcohol is on the higher centres of the brain and is manifested by a blunting of the finer grades of judgement, reflection, observation and attention. If we had sufficiently sensitive tests to measure the decrease in reflex irritability, the slowing of muscular movement and control, then the drinker even at this early stage would possibly come within the definition, because, probably, his ability to drive would have been lessened to some degree.

The Second Stage.

The second stage emerges after moderate doses when the changes already referred to become somewhat more marked. The pupils may be dilated; the eyes may glisten; respiration and heart are accelerated; the skin is flushed over the face and hands, while muscular coordination is impaired.

At this stage many persons can still reassert their self-control should the occasion demand—especially if it is a result of an accident or arrest. Apparently Dr. McGeorge (THE MEDICAL JOURNAL OF AUSTRALIA, January 24, 1942) had these two stages in mind when he wrote: "Judgement is impaired at an early stage, with deficiency of concentration . . . and most important of all, in the power of estimating risk. The last is the more serious because intoxication may not be obvious, but recklessness and the consequent danger to the safety of others may be at its greatest."

All persons when they reach the second stage are "under the influence" both legally and medically.

The Third Stage.

With larger doses the false symptoms of stimulation tend to subside and incoordination becomes more prominent. At this stage, and in the fourth stage of apathy and stupor, the condition of the imbiber is obvious and presents no legal or medical problem.

The task of the medical practitioner is indeed a difficult one, and until such time as his evidence is backed by some scientific tests then we must expect to see that unedifying spectacle of the "battle of the experts" which does so much harm to the profession. In Norway, where there is a combination of clinical examinations and blood tests, the medico-legal experts never appear for any of the parties (prosecution or defence), but always for the Court, so that this "battle of experts" is unknown.

The question: "What can be done by the practitioner to remedy this state of affairs?" can now be posed. But first of all let us recall that some medical writers have said "within the range of forensic medicine, there is no subject upon which medical evidence is more unsatisfactory than that appertaining to drunkenness", and let us consider some of the evidence given by doctors in these cases.

CASE I.—Doctor A stated: "I examined the defendant. I noticed he had obviously been drinking and smelt of liquor. His reflexes were slow. His coordination was good. There was no incoordination. He did not stagger. In my opinion he was not affected by liquor."

CASE II.—Doctor B stated: "I gave the defendant the usual tests. One of them I always give is to get the patient to close his eyes and I then push him."

CASE III.—Doctor C stated: "I could not smell liquor on the defendant. I did not ask him if he had partaken of alcohol. I gave him the usual tests and he appeared to do them reasonably well. In my opinion he was reasonably sober."

CASE IV.—Doctor D stated in answer to the question whether, in view of the lapse of time since the arrest and the medical examination, the defendant could exhibit all the symptoms of being "under the influence" at the time of arrest, and could appear sober at the time of the medical examination, he could give an opinion as to the defendant's condition at the time of arrest: "The defendant told me he had urinated several times since his arrest and prior to my examination and he would thus eliminate all the alcohol he absorbed in his urine."

Case after case on these lines can be quoted, and one golden rule emerges, and this is that the medical practitioner, when he places himself before the Court as an expert, must be fully conversant with the action of alcohol on the human organism, its absorption, oxidation or excretion. Other rules come readily to mind. For instance, the doctor should place himself in possession of all the facts (and he can do this only by questioning the patient), especially as to the times at which the patient says he has consumed liquor. One doctor informed me that his practice was to ask the police details of the accident or offence, question the defendant as to liquor consumed, apply the usual tests and give his opinion after considering all these matters. This practice has much to commend itself.

The practitioner should make full notes of what the patient tells him, of the tests he conducts, and of the result of each test, and his opinion should be based on all these factors. He must throw aside the "either drunk or sober" philosophy and remember there are varying stages between these two conditions. He must remember that the time of his examination in relation to the time when the offence occurred is always a primary issue; that no matter by what side he has been called, he will, in all probability, be required to undergo a most vigorous cross-examination by gentlemen who are more than conversant with the subject, and he must be ready to give a full and lucid explanation of any phase of the subject on which he may be questioned.

In some parts of New South Wales, practitioners will not attend in these cases unless the person calling them agrees to a blood or urine test. A combination of the clinical examination and the blood test might be a happy solution of the problem.

A. E. STONHAM, Stipendiary Magistrate,
Sydney.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on May 28, 1953, at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, DR. A. J. MURRAY, the President, in the chair.

Vertigo.

DR. R. J. MACKAY read a paper entitled "Vertigo" (see page 361).

DR. C. B. HUDSON read a paper entitled "Vertigo" (see page 363).

DR. E. P. BLASHKI referred first to the effect of streptomycin in producing vertigo. He said that it had to be remembered that streptomycin acted on both labyrinths, and that therefore while it might produce dysfunction of the two labyrinths it might not produce vertigo. Referring to the duration of vertigo, Dr. Blashki said that in the case of a lesion which destroyed one labyrinth, vertigo was due to the unopposed action of the other. After a period of a few weeks the nucleus of the vagus refused to respond any more, so that the vertigo disappeared; in the case of travel sickness the duration might be even shorter. However, it had to be remembered that a patient whose labyrinth on one side had been destroyed either by disease or by operation did not react normally to a turning stimulus; many such patients found themselves giddy on movement for a longer or shorter period. One labyrinth did not always satisfactorily take over function. Dr. Blashki said that the testing of function in the manner of Fitzgerald and Hallpike, while widely accepted, was not universally accepted. One of the leading objectors to it was Kobrak, who said that Hallpike overwhelmed a labyrinth by testing it with an overwhelming stimulus. He also said that the testing of a labyrinth with a sub-minimal stimulus produced no nystagmus which was not visible. If one labyrinth was stimulated for five seconds and the other for five seconds, a response would be obtained because there was a sort of preparedness induced by the sub-minimal stimulus. Dr. Mackay had said that obstruction of the Eustachian tube to cause vertigo must be absolute. Dr. Blashki pointed out that even so, it need not be continuous. It was possible to have a nasal deformity and defect that caused obstruction only for short periods. Dr. Blashki remembered a patient some years earlier, a commercial traveller, who every time he went to the Blue Mountains suffered from severe giddiness and nystagmus on his return to Sydney. The condition was due to obstruction of the Eustachian tube, which occurred intermittently and produced that profound result. Dr. Blashki then referred to vertigo of toxic causation, which had been said to clear up in a few weeks; he said that he had encountered cases of vertigo of toxic origin in which function had never been restored at all. The nerve lesion might not be complete at once. He had recently examined a young man, aged about twenty-seven years, who became suddenly deaf overnight after an attack of influenza. He still had a response to stimulus by the caloric test. Then he had an attack of violent vertigo which incapacitated him for a couple of days, and afterwards was still deaf in the affected ear and gave no response to the caloric test. Dr. Blashki went on to say that the theory of focal infection was now unpopular. Wright of Bristol had made much of it. Dr. Blashki thought that it should not be discarded altogether. A patient who recovered from vertigo after the removal of an infected tooth or tonsil would be grateful. One type of vertigo to which reference had not been made was that kind of "positional" vertigo which affected people when they were turning in bed. Dr. Blashki thought it was of toxic origin.

DR. JAMES ISBISTER referred to the confusion amongst both patients and doctors about the terms "dizziness", "giddiness", and "vertigo". He said that he had looked up their definitions in a medical dictionary, and had come to the conclusion that they all meant the same thing. However, it was important to be sure of one thing, whether the patient had faintness or vertigo. In faintness the patient would have clouding of vision, and in vertigo a real sense of rotation.

DR. NOEL KIRKWOOD asked what was the actual physiological cause of vertigo. He wondered whether it could be caused by suppression of stimuli from one side, or whether it needed positive abnormal stimuli.

DR. VOLNEY BULTEAU said that the distinction between whether the patients felt that they were rotating round objects or that objects were rotating round them seemed pointless. One useful means of determining whether a true rotatory phenomenon was present or not lay in the use of the caloric test; it would show whether the patient's reactions to the test were similar to those he experienced during his attacks. It was possible to compare the findings on the two sides. Referring to cervical sympathectomy, Dr. Bulteau said that it was one of the operative measures in relation to Ménière's disease which were coming into prominence, but it was not fully evaluated. It was advocated by Garnett Passe in England, and probably had its best place in the treatment of middle-aged patients who still had some hearing. The young person with some hearing left and severe vertigo was in a bad plight. The operation main-

tained the hearing and in some cases improved it, and abolished or at least reduced the giddiness.

DR. GEORGE SELBY said that one of the speakers had mentioned that nausea and vomiting were probably due to a spill-over from the labyrinthine nerves to the vagus. Dr. Selby felt that such a neuronal spill-over was unlikely on physiological grounds, and that it would not explain why patients with central nervous vertigo still experienced nausea and vomited with their attacks. Reflex connexions were thought to exist between the vestibular nuclei and the hypothalamus and reticular substance, which would appear to provide a more physiological explanation for this phenomenon. Referring to the good results claimed after excision of the stellate ganglion, Dr. Selby said that he wondered whether these were due to an improvement in the vascular supply to the labyrinth, rather than to a direct effect on the labyrinth or labyrinthine nerves. He asked also whether anyone had tried the effect of a series of stellate ganglion blocks before resorting to the more radical method of excision.

DR. D. V. GIRI said that catarrhal deafness due to blockage of the Eustachian tube was said to cause vertigo, yet many patients with catarrhal deafness had not vertigo. He wondered how that was accounted for.

DR. O. SCHMALZBACH said that he had been pleased to hear psychosomatic causes of vertigo mentioned. He had recently examined a woman, aged thirty-eight years, who had complained of vertigo for two years after her marriage. She had had an argument with her husband and left him, and had started proceedings for divorce. She had been completely investigated for other causes of her vertigo, with negative results. It was of functional type.

DR. S. BENEDEK asked how toxic epidemic vertigo was to be treated. He said that all patients with vertigo in psychiatric practice said that if their worries would stop their vertigo would stop.

Dr. Hudson, in reply, said that he had not given a definition of vertigo, but had quoted definitions given by others. He said that he was rather confused by the term and, like Dr. Isbister, had looked it up in several dictionaries. The Oxford Dictionary virtually stated that dizziness was vertigo and vertigo was dizziness. Dr. Isbister had mentioned the need to make the distinction between faintness and vertigo. This need did exist, but it was a fact that syncopal attacks might be associated with severe vertigo. On the other hand, conditions which produced vertigo might, in their mildest form, produce only a sense of insecurity. In reply to Dr. Kirkwood, who asked about the physiology of vertigo, Dr. Hudson said that he was not very competent to answer that question. Most of the conditions giving rise to vertigo resulted in a lack of balance between the labyrinthine systems; vertigo occurred either because there was impaired function on one side, or because the labyrinth on one side was stimulated. In Ménière's disease it had been postulated that hydrops of the labyrinth was actually present, but it had also been suggested that, in that condition, the labyrinth was stimulated by repeated rupture of herpetic vesicles.

Dr. Mackay, in reply to Dr. Blashki's remarks about positional vertigo and the patient turning over in bed, said that he had been referring only to paroxysmal positional vertigo when he said that the nystagmus could be produced only the first time. With regard to the cause of the vertigo, Dr. Mackay said that the theory was in general that there were tonic impulses from both labyrinths. The labyrinths were like the twin engines of an aircraft, and everything was all right if they were going along smoothly; but imbalance gave rise to symptoms. If the imbalance did not vary, the patient was ultimately able to stabilize himself, but if it kept altering he could not. That was why the patient with Ménière's disease kept on getting attacks. Dr. Mackay said that the suggestion that stellate ganglion block should be tried was a very good one; but Ménière's disease was characterized by such long remissions that one probably would not know from the block whether the patient was having a remission or not. On the subject of functional vertigo, Dr. Mackay said that he thought an organic lesion was nearly always present, even if it was very mild. If vertigo was continuous for a long time, there was a large functional element. Referring to epidemic vertigo, Dr. Mackay said that recovery occurred without treatment within three weeks.

Dr. Murray, from the chair, thanked the speakers for their papers, which had covered the subject excellently.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

A QUESTIONNAIRE FROM ENGLAND.

THE Secretary of State for the Colonies wrote under date May 31, 1829, to Lieutenant-General R. Darling, Governor of New South Wales, forwarding a *questionnaire* he had received from the Royal College of Physicians of England seeking information regarding health conditions in New South Wales.

Governor Darling instructed (A) James Bowman, Inspector of Hospitals, and (B) his deputy, Donald McLeod, M.D., to supply appropriate answers. McLeod seems to have taken his task more seriously than his principal did. Their replies, which are not always in agreement but are occasionally complementary, were included in dispatches sent to London by Darling on February 17, 1830.

Replies to Questions Proposed by the Royal College of Physicians of England.[1]

Sydney.

1. *What is the population of the Place?*

(A).

Males.			Females.			Grand Total.
Under 12.	Over 12.	Total.	Under 12.	Over 12.	Total.	
2,835	24,776	27,661	2,936	6,051	8,987	36,598

(B). The fullest information that can be afforded on the subject will be found in the appended census. The general opinion is that the population is considerably greater than is here stated and I am inclined to entertain a similar opinion.

Males.			Females.			Grand Total.
Under 12.	Over 12.	Total.	Under 12.	Over 12.	Total.	
2,835	24,776	27,611	2,936	6,055	8,991	36,602

2. *What proportion do the human deaths bear to the population?*

(A). The proportion of deaths must for many years appear to be much greater in this colony than in the old-established countries where the inhabitants are encouraged to emigrate. The number of convicts and emigrants annually sent here is very considerable, few of whom leave the colony, therefore the number of deaths will for some time exceed the births. In consequence of a great extent of this Territory being thinly populated a current Register of Births and Deaths cannot be kept especially in remote places in the interior.

(B). It is utterly impossible to answer this question with accuracy, but from particular attention to the question for the last nine months my results are nearly 1/63. Could I only procure Tables of Marriages, Births and Deaths from the Archdeacons Courts so long as such records have been kept, this question could be answered with tolerable precision. Applying the question to the Military and their Families the proportion would be nearly 1/75.

3. *Are there any remarkable instances of longevity amongst the inhabitants?*

(A). The colony having been established in 1788 does not afford sufficient data to enable me to answer this question. Many of the Black Natives who were children at that time (42 years ago) appear old and infirm now; therefore I pre-

[1] From the original in the Mitchell Library, Sydney.

sume longevity is not commonly known among that race of inhabitants.

(B). The appearance of some Blacks about 180 miles west of Bathurst in the neighbourhood of the Murrumbidgee River who have not been debased by intercourse with Europeans warrants the assumption that they are 65 or 70 years of age and are likely to form a perfect contrast with the natives of the same age near the coast. Only one native was found with the scabbed head in a journey of 500 miles whilst in Cumberland almost every other black will be labouring under this loathsome disease. The recent colonization of the colony prevents any particular and striking instances of longevity from coming under notice. Whether the Colonial Youth will be long-lived or not is a question that only time will show. Many believe they will not arrive at an advanced period of life whilst others entertain an opinion entirely opposite. The Benevolent Asylum may be considered as affording the best information on this subject. At this time there are upwards of 100 inmates, the third of whom are upwards of 70 years of age—some have reached 90 and one is 103 years of age. Of these five came in the first Fleet. One of the first Fleeters died a few years ago at the advanced age of 104 years without having lost a tooth or a hair of his head being grey. His wife is still living aged 96 and can see to read moderately small print and hem the border of a cap without the aid of glasses. There are great numbers of men and women that are certainly upwards of 70 who are capable of performing ordinary field labour and going long journeys in the woods. In the Windsor Burial Ground, of the men and women who could afford to have a stone placed over their graves there are eight from 50 to 60, nine from 60-70, two from 70-80 and one 98 years of age when they died.

4. *What are the features, colour of the hair, and average stature of the Aborigines?*

(A). The question I presume alludes to aborigines only. Their features are very different in the various tribes on the coast and in the interior—most of them are coarse and irregular. Their complexion and hair black—the average height of the men on the coast is 5 feet 9 inches. In the Mountain Districts many of them are considerably shorter and more muscular, evidently capable of more exertion.

(B). The features of the Aborigines are far from being pleasing. The facial angle is little different from that of the Hottentot. The eyebrows are large and bushy: the cheek bones high, the nose flat, the nostrils large, the eyes thick, teeth strong and almost universally of a beautiful white colour: the beard is something partially scattered over the face, but is always strong, complexion of a deep dun colour. Hair universally black except in cases of age, generally strong and straight particularly among the females. The average stature of the man is 5 feet 6½ inches, of the women 5 feet. A considerable difference of stature is observed between the tribes on the coast, in the towns and far in the interior. On the Coast they are generally tall, thin and active, in the towns diminutive and emaciated, in the Country about Bathurst and Argyle they are well proportioned and beyond these countries Captain Sturt of the 39th Regiment in his journey to explore the Interior met with natives more wretched than those even about the towns. The women universally are low in stature and perhaps the average of five feet is too high.

The British Colonial natives have fine open pale and lively features generally, fair complexion and light hair in early life, after puberty it becomes dark. The average stature of the male is 5 feet 9½ inches and the females 5 feet 4½ inches.

5. *What is the mean height of the thermometer in the summer and winter months?*

(A). From several years' observation the medium height of the thermometer at Sydney is 63½°. At the other stations there has not yet been sufficient attention paid to the thermometer to make a correct statement.

(B). The mean temperature of the year is about 64° of Fahrt. June, July and August are the months that show the greatest cold in Sydney, but in these months the thermometer falls to 20° lower in Parramaatta than in Sydney. January and February are the hottest months in Sydney, as also in Parramatta, but in the latter place the mercury rises nearly 20° higher than in the former. The greatest cold observed in Sydney in the years 1821-27-28-29 was 48°, 51°, 40° and 52° respectively. In Parramatta the greatest cold observed in the years 1822-23 and 29 stands at 27°, 28°, 27°. The medium range, however, of cold does not exceed 7° on the average in Sydney; the average temperature of the spring months is 65·5° in Sydney: the same months at Parramatta 67·3°. Summer temperature—in Sydney 72°, in Parramatta 74°. Autumn 66° in Sydney, 59·6° in Parramatta. Winter 53° in Parramatta and 55° in Sydney. The mean average of five years' observations makes the temperature 65·2°.

6. *From what quarters do winds chiefly prevail and during what months?*

(A). The surveyors have observed on all places on this Island the winds prevail from the sea in the summer. On this part of the coast the sea breeze is about north east and the reverse on the opposite side. In winter the winds are very variable, from the south and frequently at Sydney very cold from the westward blowing over the mountains.

(B). Deductions from twelve months' observations noted three times a day shows that westerly winds prevail. Four years of subsequent observation confirms the fact.

7. *What is the nature of the soil?*

(A). There is a great variety of soil in the Interior fit for every kind of culture—about the coast it is chiefly an unproductive clay.

(B). Every variety is to be found in the County of Cumberland from sand to the richest alluvial deposits. The neighbourhood of Sydney is generally poorer, but as we retire from the coast the country improves. Ironstone, gravel, common sandstone rocks together with blue and grey chisms are very common materials. At Prospect Hill, One Tree Hill and Corne's Hill we meet with whinstone, but everywhere else the lower part of the country is one uninterrupted mass of siliceous sandstone. Were the seasons only regular there is soil adapted to all the purposes of agriculture.

8. *Are there any mineral springs there? If so, are they saline, chalybeate, sulphurous or of what nature?*

(A). None.

(B). There are brackish springs in every part of the County of Cumberland, but they are far less found in the adjoining counties. Aluminous springs or more properly speaking collections of water impregnated with alum are frequently to be met with in Argyle, but whether these are springs of this nature or the water has been impregnated by running over aluminous earth has not been ascertained.

9. *What are the medical substances in the colony and how are they prepared?*

(A). Many medicinal plants might be cultivated in this climate with great advantage.

(B). There are none that have been received into the Pharmacopœia. Specific mention is made of the essential oil of the Peppermint tree Eucalyptus peperita by Dr. White in his book. The gum of the grass tree Lanthorea hostile of Brown is said by the same gentleman to produce good effects in chronic affections of the bowels, but neither the above medical substances nor others that might be enumerated have ever come into repute among regular practitioners: not that they are undeserving of attention, but because from one cause or another their specific natures and their particular adaption to the alleviation or cure of diseases have not been investigated.

The gum of the Green Wattle (mimosa decurrens) and a decoction of the bark of the Willow (mimosa longifolia) as popular medicines in cases of Dysentery and Diarrhea are in high repute and in some stages of this disease I have no doubt are of some efficiency. The question requires much time and means and opportunities of making experiments before any definite answer can be given. General replies to such a question are of no utility. As experiments have rarely been made except in the popular articles I have mentioned which are alleged to have produced wonderful cures. I have only further to add that I have long been using all the means in my power to acquire a definite and distinct knowledge of the medical substances of the colony, but I am far from being ready to give the results to the public because I am not satisfied with them myself.

(To be continued.)

Correspondence.

METHYL N-PROPYL ETHER.

SIR: Early in 1950 I endeavoured to obtain some methyl n-propyl ether, but was unable to do so because of import restrictions. I am writing now to let anyone who is interested know that this anæsthetic agent is now available.

H. Bleakley and Company, of Melbourne, were good enough to supply me with a trial quantity (through Dr. James, of the Royal Melbourne Hospital). My experiences with it are not original or extensive enough to justify my writing a paper, but I would like to say that its properties were as described in a paper by C. E. Sykes (*Brit. M. J.*, August 20, 1949). Briefly, methyl n-propyl ether differs from its isomer di-ethyl ether in that it has a different smell, is somewhat more potent, has a less irritant effect on the bronchial tree (with less tendency to produce coughing during induction of anæsthesia), and a slightly less tendency to cause headache and vomiting post-operatively. It is, of course, inflammable, and occasionally muscular tremors occur during emergence. Methyl n-propyl ether is more expensive than di-ethyl ether; but this is not of great importance if administration is carried out by a closed carbon dioxide absorption method.

Yours, etc.,

1 Uplands Road,
North Balwyn,
Victoria.
August 19, 1953.

W. H. J. COLE.

BLOOD IN THE ALVEOLI AND BRONCHIOLES OF NEW-BORN INFANTS.

SIR: In the recently published "Pathology of the Fœtus and the Newborn" (1952), by Edith L. Potter, of Chicago, at page 257, it is stated that diffuse intraalveolar hæmorrhage may be seen in infants a few hours to a few days old and is the most difficult form of hæmorrhage to interpret. It is found more commonly in infants three to five days old, and in these cases it has been variously interpreted but apparently not very satisfactorily. A hæmorrhagic form of pneumonia has been suggested, and also a hæmorrhagic condition due to hypothrombinæmia. The presence of red cells in groups of alveoli and also often in the bronchioles in nine cases out of 27 autopsies on infants carried out at Mareeba Babies' Hospital, Adelaide, commencing June 1, 1945, and ending in September, 1946, seems more likely to have been due, in some of the cases at least, to the inhalation of blood than to the above suggested causes. Mareeba receives sick babies from various maternity hospitals and other sources. At the time it was hoped that more complete clinical details and histories would be obtained, but this is no longer possible. The important matter is that in such a large proportion (one-third) of these infants, blood, possibly inhaled blood, should be present in a sufficient number of alveoli to give rise to purple patches in the lungs or to dark red areas of consolidation. The condition was sufficiently extensive, in some instances, to have been responsible for the fatal issue and in others it probably contributed to this. The impression given was that blood had probably been inhaled. Red cells could often be found in the bronchioles in the affected region, and the appearances presented were similar to those cases—for instance, deaths from accidents—in which it has been known that blood had been inhaled. If the red cells in the alveoli had escaped from the capillaries in the wall as a result of intense congestion, one would hardly expect frequently to find hæmorrhage also in the smaller bronchioles. It is this feature which made us think that blood had been inhaled, and that possibly some new factor was operating over this period in the management of infants which led to bleeding in the oral cavity or the upper respiratory tract. If this condition previously had been of frequent occurrence in young infants, it could hardly have escaped notice. If, for instance, it was due to the inhalation of blood during birth, as in breech cases where a respiration may occur before the child is completely born, then these cases should have been often observed before. We made such inquiries as were possible and discussed the matter with Dr. W. F. Joynt, then the Director of Obstetrics. In one of our cases hæmorrhage had followed gavage, and we think in that case some slight trauma must have occurred, thus explaining the inhalation of blood into the lungs. Dr. Joynt suggested the possibility that suction applied to new-born infants to clear mucus from the upper respiratory passages might, in some cases, lead to small hæmorrhages from which blood might be inhaled.

It will be seen from the above that we were by no means acquainted with the cause of the condition; but we believed that it was due to inhaled blood rather than to the escape of blood from congested capillaries in the alveolar wall.

The ages of the patients were three, four, five, seven days, three weeks, twenty-four days, one month, and nine weeks. In nearly half the cases the infant's death took place within the first week after birth, but in some instances, in which the blood did not become absorbed and there were probably secondary reactions in the lungs, death did not occur till from three to nine weeks. In the three weeks old baby the red cells were packed together and had shrunk from the alveolar wall, and there were some polymorphs amongst them. In the nine weeks old infant some of the alveoli were filled with apparently fused red cells forming red reticulated patches in which polymorphs lay in vacuoles; some of the red cells had lost most of their hæmoglobin.

Yours, etc.,

University of Adelaide,
Adelaide,
August 13, 1953.

J. B. CLELAND.

PINK DISEASE.

SIR: I read with interest the letter by Dr. Ellen Kent-Hughes regarding pink disease (July 11, 1953, issue). She states that over a period of twenty years she has found that the elimination of milk in the diet is of benefit. The only patient that Dr. Hughes has lost was one that received added salt in the diet and developed gangrene of the buttocks. The implication here (if I understood correctly) was that a high salt diet was causally related to the death of this child.

Four years ago I submitted evidence that children suffering from pink disease were deficient in sodium and chloride. Over one year ago I reviewed our understanding of this disease (Cheek, 1953), and I presented detailed electrolyte studies from one case. Since then I have investigated two other cases in detail.

It can be stated, without resort to hypotheses, that there is a significant disturbance in electrolyte and fluid balance. There is a loss of cell potassium and the replacement of this ion by sodium. Metabolic alkalosis is present, and there is reason to believe that hydrogen ion is transferred to the intracellular compartment (Cooke, Segar, Cheek, Coville, and Darrow, 1952; Orloff, Kennedy, and Berliner, 1953). By comparison with normal children there is about a 30% reduction of total body chloride and of extracellular water. There is a loss of total body water and of plasma volume. These changes are associated with a rise in venous pressure, and in one case it has been possible to demonstrate a reduction of glomerular filtration.

I have found that children in states of poor nutrition demonstrate an expansion of extracellular water and an increase in total body chloride.

Starvation leads to a decrease in intracellular water and to a loss of body fat. Expansion of the extracellular water and elevation of total body chloride therefore result.

The significance of this low total chloride in pink disease is thus even further enhanced when we consider these relevant facts.

No clinical improvement or reversion to a positive nitrogen balance need be expected while this parlous state exists. It must be emphasized that the serum chloride concentration is no index as to the status of total body chloride (Cheek, 1953, in preparation). In the past this fact has obscured our appreciation for the changes of electrolyte balance in pink disease.

The cause of this departure from homœostasis cannot be discussed here—suffice it to point out that there is an alteration of kidney function. Balance studies reveal that the correct approach, which favours the restoration of electrolyte equilibrium, is the administration of potassium chloride. This can be given in orange juice, which in itself is a rich source of potassium. To this glucose, or a simple carbohydrate, should be added. The administration of potassium chloride will result in a restoration of cell potassium and a return of sodium to its rightful place in the extracellular fluid. Chloride retention with reexpansion of the extracellular fluid will occur. However, there may be continuous and large losses of chloride in the sweat which are not easily replaced.

Additional potassium chloride and small amounts of sodium chloride should be added to the fluid intake of patients with pink disease. This should lead to improvement in the clinical condition and finds a scientific and physiological foundation. The administration of sodium chloride alone does not find a satisfactory physiological basis.

The greatest water expenditure is in the form of sweat and insensible water loss. Only 30% or less of the fluid intake is available for excretion as urine. This is of importance. In the early stages, forced feeding with foods containing a high nitrogen content without adequate glucose and water will provide a high solute load which the kidney is unable to excrete effectively. This will produce a further deterioration of hydration. This danger has been demonstrated in normal infants who are not even subject to excessive sweat loss (Pratt and Snyderman, 1953). I suggest that the observations of Dr. Kent-Hughes find explanation

on this basis. Cognizance must be taken of the protein-sparing effect exerted by glucose (Gamble, 1951). Three grammes of glucose per kilogram not only produce an anti-ketogenic effect, but diminish losses of protein in the fasting patient. Moreover, glucose will reduce the solute load on the kidney and will thus economize on water and electrolyte expenditure.

The results of my investigations will be published at a later date.

Yours, etc.,

DONALD B. CHEEK,
Research Fellow, Department of Pædiatrics, University of Toronto; Hospital for Sick Children, Toronto.

August 14, 1953.

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A METHOD OF GROWING MYCOBACTERIUM TUBERCULOSIS.

SIR: With the consent of the Chairman of the Repatriation Commission, the yolk sac method for growth of *Mycobacterium tuberculosis* as outlined by Brueck and Buddingh has been investigated at the Repatriation General Hospital, Heidelberg.

For an unselected group of cases a preliminary report can be furnished for general information.

The work was undertaken by Miss Dorothy Mountford, who states that:

"Isolation of M. Tuberculosis by Inoculation of the Yolk Sac of Embryonated Eggs. Brueck and Buddingh (*Proc. Soc. Exper. Biol. & Med.*, 1952, 589) described in a preliminary report a method for the isolation of *M. tuberculosis* from materials collected from tuberculous patients. They used materials in which a thorough search failed to reveal the presence of acid-fast bacilli by microscopic examination (including concentration procedures). It was not stated whether these patients were receiving chemotherapy.

"Their technique was repeated accurately in this laboratory with specimens of sputum from known tuberculous patients. Briefly the method consists of digesting the specimen with 4% caustic soda, neutralizing, and resuspending the deposit in a solution of penicillin. 0·2 ml. of this suspension is inoculated into the yolk of six day old embryos, six eggs per specimen are inoculated. The eggs are incubated at 37° C., and the embryos alive after four days are examined daily for acid-fast bacilli. To do this some of the yolk is extracted with 15% phenol, and a smear of the fatty layer examined for acid-fast bacilli. However it was found more satisfactory in this Laboratory to extract the yolk with xylol. The acid-fast bacilli in the yolk sac are then identified as *M. tuberculosis* by injection of the yolk into guinea-pigs. We, however, subbed the yolk sac onto tubes of Löwenstein media and examined these for the time and type of growth of *M. tuberculosis*.

"Brueck and Buddingh claim that the yolk sac technique provides favourable conditions for the rapid proliferation of *M. tuberculosis*, and that they are demonstrable six days after inoculation. They examined various specimens in this manner from thirty-nine tuberculous patients, and in all thirty-nine cases *M. tuberculosis* was demonstrated. That is, in 100% of cases they could not demonstrate *M. tuberculosis* by the slide technique, but they were demonstrable by the egg technique.

"Brueck and Buddingh's methods did not appear to be a true comparison, since they were comparing a culture technique with a slide technique. For this reason the treated sputa were inoculated on Löwenstein media in addition to the eggs. The results from thirty cases are shown in the following table.

A. Number of positive smears	Number of positive growths in eggs	Number of positive growths in culture.
4 (2 on chemotherapy)	4 positive on 7th day after inoculation	All positive within three weeks
B. Negative smear.	Positive egg	Positive culture
2	2 positive on 7th day	2 positive within 3 weeks
C. Negative smear	Positive egg	Negative culture
3 (1 on chemotherapy)	3 positive 7 days	3—no growth after 6 weeks
D. Negative smear	Negative egg	Positive culture
4 (1 on chemotherapy)	Negative after 14 days	Positive within 3 weeks.
E. Negative smear	Negative egg	Negative culture
15 (5 on chemotherapy)	Negative after 14 days	Negative culture after 6 weeks

"The cultures inoculated from the egg sac for confirmation were all typical of *M. tuberculosis*.

"It appears from these results that 13% more positives grew on the media and not in the eggs. (In routine work in this Laboratory it is found that 16% of the positive cultures have negative slides—calculated from five hundred cases.) 10% more positives grew in eggs and not on the media.

"No *M. tuberculosis* could be detected in eggs before the seventh day and all the positives were detectable by the tenth day. All the cultures had grown within three weeks (this is also found in routine work).

"Thus the advantage of the egg technique appears to be that a preliminary result can be given ten days earlier, although another three weeks is required for confirmation. However, this method requires a great deal more time to perform.

"It is obvious that a much larger number of specimens would need to be examined before this method could be assessed accurately. It was also found very difficult to select tuberculous patients with sputum negative on direct smear but positive on culture, as was apparently done by Brueck and Buddingh."

In brief, it would seem that the method will accurately reproduce the results given by cultures and in a much shorter time. Whether the increased cost in materials and equipment would justify adoption is a matter for individual assessment.

Yours, etc.,

R. B. MAYNARD,
Senior Specialist Medical Officer (Pathology).
Pathology Department,
Repatriation General Hospital,
Heidelberg West,
Victoria.

July 29, 1953.

COMPULSORY CHEST X-RAY EXAMINATIONS.

SIR: I was very interested to read Dr. Rubinstein's letter (M. J. AUSTRALIA, August 1, 1953) criticizing me for some of my statements in the journal of July 11, 1953.

I was particularly interested in his "typical case"—a completely asymptomatic case of tuberculosis picked up by the mass survey and now in hospital being "saved by the skill and attention of doctors and nurses". According to Dr. Rubinstein, her condition was apparently perfectly healthy on examination before "treatment", and I feel confident that she will make a "wonderful recovery".

Dr. Wilson accuses me of a "flagrant contradiction", because I stated that tuberculosis required no treatment unless it caused ill health, and later said that tuberculosis was most amenable to treatment in its early stages. Surely Dr. Wilson admits that most people contract a tuberculous infection and

overcome it without becoming ill. It is the relatively few whose resistance breaks down that become ill, and this may, and often does, occur in the early stages of the infection.

Where is the contradiction?

Dr. Wilson writes (M. J. AUSTRALIA, August 1): "Symptoms of ill health are, so far as tuberculosis is concerned, preceded usually by extensive lung pathology which is more often than not irreversible." This may be true, but Dr. Wilson must admit that it is quite common to find radiological evidence of quite extensive irreversible lung pathology in people who are perfectly well and have always been perfectly well and continue to remain perfectly well, and whose chest X-ray appearances remain unchanged over years.

Did these people require treatment? And yet their serial X rays are often comparable with those of treated cases, including people who became ill.

Is it not the breakdown of resistance that makes people sick? And as regards both treatment and prevention, is it not more logical to concentrate on those with symptoms who are both in need of treatment and spreaders of the disease?

Dr. Wilson assures me that his X-ray plant is not deterred by such usually radio-opaque things as "falsies", buttons *et cetera*. This is hard to reconcile with the fact that it is customary at his clinic, when taking full-size follow-up X rays, to strip the patient to the waist, or in the case of women, to allow a cotton gown only.

It would appear then that Dr. Wilson is more fortunate in the interpretation of his miniature X-ray films than of his full-sized ones.

Dr. Wilson also states that: "If we were to stop X-raying . . . the number of undiscovered cases would be building up to such proportions that within a few years we would have an incidence of the disease that would make even the staunchest of us tremble."

I find this hard to reconcile with the fact that there has been a steady decrease in the mortality from the disease for many years preceding mass radiography.

Yours, etc.,

21 Condon Avenue,
Cessnock,
August 14, 1953.

B. SHORT.

Obituary.

FREDERICK ARTHUR MAGUIRE.

DR. FREDERICK ARTHUR MAGUIRE, whose death was announced recently in this journal, was a man who achieved distinction in many walks of life. He entered more fields of activity than most of his colleagues, and rose to prominence in all of them. This seemed to happen quite naturally, for he had many gifts in addition to a commanding presence and a large, resonant voice, which he knew how to use. If he had entered politics, he would have found it useful on the hustings.

Arthur Maguire, as he was known to most of his friends, was born on March 28, 1888, at Cobar, New South Wales; he was the son of a schoolmaster, and no doubt inherited from his father some of his teaching ability. He went to school at the Sydney Grammar School, and studied medicine at the University of Sydney, graduating as bachelor of medicine in 1911. He did not take out his Ch.M. degree until 1919. He obtained the degree of doctor of medicine in 1926.

Immediately after his graduation Maguire was appointed resident medical officer at the Royal Prince Alfred Hospital, and thus began an association which ended only with his death. In 1912 he was appointed demonstrator in anatomy at the University of Sydney. In 1914 came the First World War. He sailed with the First Expeditionary Force to New Guinea. The late Neville Howse was principal medical officer, and Maguire, with the rank of captain, was his second in command. As soon as matters had been put in order in New Guinea, Howse obtained permission from the Administrator to return to Australia, so that he might enlist in the Australian Imperial Force. He left Maguire behind him as principal medical officer. This position he held from October 12, 1914, until February 25, 1915, when he in turn returned to Australia. At this time the late R. H. Fetherston was Director-General of Medical Services, and Maguire was appointed his full-time medical staff officer. Fetherston and Maguire did an enormous amount of work between them. No doubt the staff should have been larger, but it is a fact that to this day there are many who speak with admiration of the work of these two men. In February, 1916, Maguire was appointed Commanding Officer of the Ninth Field Ambulance in the Australian Imperial Force. He held this command until January, 1918, when he was appointed A.D.M.S. of the Third Division of the Australian Imperial Force, a position that he held until April, 1920. For his work in France he was mentioned four times in dispatches and received the Distinguished Service Order. In the interval between the two World Wars, Maguire held the position of Deputy Director of Medical Services of the Second Military District (New South Wales) on two occasions, from August 1, 1921, to August 31, 1933, and from March 1, 1934, to December 31, 1934. From July 1, 1935, to June 30, 1939, he was Honorary Surgeon to His Excellency the Governor-General. During the Second World War Maguire succeeded the late Rupert Downes, Director-

General of Medical Services, on March 26, 1941; he was given the temporary rank of Major-General. He served in this position until April 5, 1942, when he retired, being placed in the same month on the Retired List with the honorary rank of Major-General.

Maguire became a gynæcologist and was appointed to the honorary staff of the Royal Prince Alfred Hospital; he rose to be senior gynæcological surgeon and was eventually appointed to the consulting staff. His practice as a gynæcologist was bound up with his service to the University of Sydney. His work as an anatomist was, as may well be imagined, of great service to him in his gynæcological work. He had gained his doctor of medicine degree for a thesis entitled "A Critical Survey of the Female Pelvis", and later on he published a book, "The Anatomy of the Female Pelvis". He also wrote on "The Anatomy of Procidentia Uteri". In 1920 he was appointed Acting Professor of Anatomy, and held the position until 1923, when he became lecturer and demonstrator in the same subject; in 1925 he again acted as Professor of Anatomy. He was subsequently senior lecturer in anatomy until May, 1926. He was an examiner in anatomy from 1920 till 1938. In 1943 and 1944 he was part-time lecturer in anatomy, and in 1928 he

was given the title of Honorary Demonstrator in Anatomy, which he held for life. From 1943 to 1948 he was lecturer in gynæcology; and he was lecturer in clinical gynæcology at the Royal Prince Alfred Hospital from 1938 to 1941, and also for the year 1943. In 1948 he was honorary lecturer in pathology. From 1934 to 1939 he was a member of the Senate of the University, having been elected by the graduates. For the same period he was a member of the Faculty of Medicine. In 1935 he was elected by the Senate of the University as a member of its Cancer Research Committee; he was its chairman from 1936 to 1938. Among the other medical appointments which he held was that of honorary consulting gynæcological surgeon to Saint Vincent's Hospital, Sydney.

He made many contributions to medical literature. He was always enthusiastic about what he did, and in the opinion of many he allowed his enthusiasm towards the end of his life to outrun his judgement; in other words, some of his geese were swans. He published observations made on certain patients suffering from malignant disease whom he had treated with antibiotics and ACTH. He felt that he should publish the results, but his enthusiasm in their presentation was perhaps not wise. This, however, should not be allowed to sully the reputation of a man who gave lifelong devotion to the progress of gynæcology, and who was concerned above all with the welfare of his patients.

Arthur Maguire was a member of the New South Wales Branch of the British Medical Association. He was a member of its Council for one year. This was in the year 1950-1951. It is in some respects surprising that he had not previously sought office, but his life was so full that perhaps such a step might have been unwise. At the Hobart session of the Australasian Medical Congress (British Medical Association), Maguire was President of the Section of Naval, Military and Air Force Medicine and Surgery. His president's address on that occasion aroused much favourable comment. He was also President of the Section of Gynæcology of the Sixth Session held at Brisbane in 1950.

Maguire was a foundation member of the Royal College of Obstetricians and Gynæcologists. He was actively associated with the inception of the Australian Regional Council of the College in 1947. He was chairman of the provisional Regional Council from 1947, but when the permanent Council was formed in 1950, he became first chairman, and held the position until his death. The Acting Honorary Secretary of the Australian Regional Council writes: "Maguire was one of the trustees of the trust fund of the College in Australia, and generally guided the activities of the Regional Council during his period of office. Recently he presented his private library to the Regional Council."

In 1949 Maguire entered the sphere of local government and became a member of the Sydney Municipal Council on January 1. He held office until December 1, 1950. As a member of the Council he was able to present medical facts to it in a suitable way when necessary.

Freemasonry claimed Maguire's attention soon after the First World War, and he was initiated in Lodge Australia, New South Wales, on June 14, 1920. He rose to office in an incredibly short time, and in 1927-1928 he was the one-hundredth master of the lodge into which he had been initiated. He was appointed Deputy Grand Master of the United Grand Lodge of New South Wales in 1930 and 1931, and in 1932 was appointed Grand Master and held office in 1933 and 1934, and once again in 1944. He was appointed Pro Grand Master to Lord Gowrie in 1935, 1936, 1937, 1938, 1939, 1940, 1941, 1942 and 1943. It was during this period that he went to England to attend the installation of His Royal Highness the late Duke of Kent; he went as representative of the Grand Master of United Grand Lodge of New South Wales. Maguire was elected a member of the Masonic Hospital Board in 1931 and a member of the School Council and a trustee in 1934. He was the representative in New South Wales of the United Grand Lodge of England.

Maguire received other honours. In 1933 he was created a Companion of the Most Distinguished Order of Saint Michael and Saint George; he was a Hospitaller and Almoner of the Priory of the Australian Commonwealth of the Venerable Order of Saint John of Jerusalem, and also a Commander of the Venerable Order of Saint John of Jerusalem. He was a Fellow of the Royal Australasian College of Surgeons, of the Royal College of Surgeons of England, of the American College of Surgeons, of the Royal College of Obstetricians and Gynæcologists, as well as of the College of Radiologists (Aust. and N.Z.). He was a member of the Board of Directors of the Royal Prince Alfred Hospital, and also of the Board of Directors of the Benevolent Society of New South Wales. For several years he undertook the abstracting of journals on gynæcology for THE MEDICAL JOURNAL OF AUSTRALIA. He did this with the efficiency that would be expected of him, possibly in the busiest time of his career. He always said that abstracting made him read carefully, and that he had to read in order to know what was going on in the gynæcological world. If at times he was a little irritable and on one occasion even explosive, this could be forgiven him because he responded at once to an explanation and a refusal to take notice of his change of manner.

The recital of Maguire's attainments has been long, and many will perhaps wonder how he managed to crowd everything into his life. He was a man with enormous drive and endurance. He had a capacity for friendship; but at the same time his friends sometimes had to make allowance for his temperament. He was generous to a degree; he was quick in action when need be, and his friends will remember one occasion on which he flew to England at a moment's notice to redress a wrong that had been done to a member of his family. While it would not be correct to ascribe to him the qualities of greatness, he was without doubt one of the most notable medical men of his period. He was married three times, his last marriage being with Dr. M. M. McElhone, who had carried out research with him.

DR. LAURENCE HUGHES writes: Arthur Maquire's life was one of unusually notable achievement. Chapter and verse for this statement is provided by the fact that he attained the highest possible status in his profession as a surgeon in the Army Medical Services and in Masonry apart from other activities. He was the very antithesis to the jack of all trades and master of none, for he was master of most of his varied interests. His splendid record is fully told elsewhere in the journal, but, after an unsullied friendship of forty-five years, it is to the man himself that I wish to pay this small but sincere tribute.

Those who knew him well and were privileged to call him friend and the very many people to whom he brought health and happiness realized his kind, loyal and generous qualities. It was inevitable that a personality of his calibre should have antagonists. He at all times had the courage of his convictions to which he applied an extraordinary capacity for work and enthusiasm which characterized his every interest.

Arthur Maguire will long be remembered as a distinguished Australian by fellow members of the profession and the general public.

VICTOR BONNEY.

DR. H. H. SCHLINK writes: Mr. Victor Bonney, M.D., M.S., B.Sc., F.R.C.S., F.R.C.O.G., died in London on July 5, 1953, aged eighty years. As one among many Australians who have benefited by the teaching, writings and friendship of this great British surgeon, I would like to pay tribute to him and express sympathy to his widow in her sorrow.

Victor Bonney was born at Chelsea, the son of a doctor. He received his medical education at Saint Bartholomew's and Middlesex Hospitals, on which he served for eight years as a registrar. As he often said to me, there is no royal road to success in surgery, but each aspirant must go through the mill of the lesser teaching positions.

But what a success rewarded his efforts! He became one of the most famous gynæcological surgeons in London. His theatre was always packed with students from every part of the world, and Bonney, by his writings alone and with Sir Comyns Berkeley, attained an international reputation of the highest order. He was joint author with Sir Comyns Berkeley of the well-known text-book "Operative Gynæcology", which did so much to raise British prestige in this branch of surgery. Bonney alone was the author of a text-book of gynæcological surgery and of numerous other writings, either alone or in collaboration with others. It is interesting to record that most of the fine drawings in these books were drawn by himself.

He was the one British surgeon who consistently practised from 1900 until his death the Wertheim radical hysterectomy for cancer of the womb and secured results which are standard even today. They are remarkable considering that he never availed himself of the pre-operative or post-operative help of radium or X rays.

He was a colossal worker and was attached to many London hospitals, chief amongst which were the Chelsea

Hospital for Women and the Middlesex Hospitals. He also served in one capacity or another on Royal Masonic, the Postgraduate Hospital at Hammersmith, the Queen Charlotte's Hospital *et cetera*.

He had a brilliant academic career and was Hunterian Lecturer in 1908, 1930 and 1931, Bradshaw Lecturer in 1934, and a member of the Council of the Royal College of Surgeons and a vice-president. He was a Foundation Fellow of the Royal Australasian College of Surgeons and attended the first meeting of the College at Canberra. He was an Honorary Fellow of the American Gynæcological Society and of the Royal College of Obstetricians and Gynæcologists and was on the Central Midwives Board.

Mr. Bonney was a kindly man and represented all that is best in British surgery. He was a great help to hundreds of Australian surgeons visiting London. He was very fond of fishing and dancing, and, being so much associated with female patients, was in the habit of calling everybody "dear" or "darling"! Well do I remember a dinner party given him by the late Sir Alexander MacCormick when he visited Sydney. Next morning Sir Alexander met me and said, "Schlink, what kind of a man is Bonney—he called me 'my dear' last evening?" I explained that Bonney called everybody "dear" or "darling" from force of habit, but he need not be afraid!

A very great man—sympathetic, kind, honest, and a first-class technician and teacher. Britain can ill spare such a man. We grateful past students of his in Australia offer his widow and relatives our sympathy in their sorrow.

Research.

NUFFIELD FOUNDATION DOMINION TRAVELLING FELLOWSHIPS.

THE Nuffield Foundation will continue in 1954 its scheme of offering a number of travelling Fellowships to Australian graduates. Seven awards will be available, including the following: two Fellowships in medicine, two Fellowships in the natural sciences, one Fellowship in the humanities, one Fellowship in the social sciences.

The purpose of the Fellowships is to enable Australian graduates of outstanding ability to gain experience and training in the United Kingdom in their chosen fields, and to make contact there with scholars working in those fields, with a view to the Fellows equipping themselves to take up senior posts in research and teaching in Australia.

The Fellowships are intended for men or women of first-rate intellectual and personal qualities, who have already shown unusual capacity to advance knowledge and teaching in one of the fields concerned. Candidates must be Australian nationals, normally between the ages of twenty-five and thirty-five years, and must be university graduates holding, preferably, a master's or doctor's degree, and having subsequently had a year or more of teaching or research experience on the staff of a university or comparable institution.

A Fellowship will normally be tenable for one year, but in exceptional cases may be extended for a further period of a few months. The Fellowship will provide for return travelling expenses of a Fellow between his home residence and the United Kingdom and, if he is married, similar expenses for his wife; an adequate allowance will be made for the Fellow's living and travelling expenses in the United Kingdom and for his academic fees, books and other incidental expenses, as well as a personal allowance. The total value of an award, including all travelling expenses, varies with the needs and family responsibilities of the holder, but will in no case be less than £900.

A Fellow will be expected to resume residence in Australia on the completion of the Fellowship.

Except with the express permission of the Trustees of the Foundation, a Fellow may not hold any other award concurrently with the Fellowship.

A Fellow will be required to carry out, at centres approved by the Trustees of the Foundation, a programme of research work and training, similarly approved. Other work, paid or unpaid, may not be undertaken without the permission of the Trustees. During the tenure of the Fellowship a Fellow will not normally be permitted to prepare specifically for, or to take, examinations for higher degrees or diplomas awarded by bodies in the United Kingdom.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED AUGUST 1, 1953.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2(1)	8(3)	..	..	..	..	..	..	10
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	2(2)	11(10)	..	..	..	5	..	18
Diphtheria	4(3)	4	11(5)	..	..	..	..	..	19
Dysentery (Bacillary)	..	..	1(1)	3(2)	8(3)	..	..	..	12
Encephalitis	..	1	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	..	22(4)	..	..	4(3)	..	..	..	26
Lead Poisoning	..	..	1	..	1	..	..	..	2
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	1(1)	..	2	..	3
Meningococcal Infection	6(3)	5(5)	1	2	1	1	..	..	16
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	13(12)	2(1)	..	7(4)	..	..	..	..	22
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	35(18)	..	..	29(19)	..	..	..	64
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	13(11)	55(34)	9(6)	9(2)	1(1)	1(1)	..	1	89
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	44(39)	16(9)	9(8)	3(3)	5(3)	9(6)	..	..	86
Typhoid Fever	3	4(4)	..	2(2)	..	..	..	1	10
Typhus (Flea-, Mite- and Tick-borne)	1	..	..	1(1)	..	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

A Fellow will be required to submit to the Trustees, at the end of the Fellowship, a report on his work during the Fellowship.

Should the Trustees at any time find that a Fellow neglects or has neglected the obligations of the appointment, they shall have power immediately to terminate the Fellowship.

The Fellowships will be awarded by the Trustees of the Foundation on the recommendation of its Advisory Committee in Australia.

Applications for Fellowships to begin in 1954 should be submitted not later than November 1, 1953, to the Secretary, Nuffield Foundation Australian Advisory Committee, c.o. The Australian National University, Canberra, A.C.T., from whom copies of the application form may be obtained.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Week-end Course at Albury.

THE Post-Graduate Committee in Medicine, in conjunction with the Border Medical Association, will hold a week-end course at the Albury Base Hospital, Albury, on Saturday and Sunday, September 12 and 13, 1953. The programme is as follows:

Saturday, September 12: 2 p.m., registration; 2.30 p.m., "Advances in Anæsthesia in General Practice", Dr. Gwen Bernard; 4 p.m., "Recent Advances in Surgical Conditions of the Colon and Rectum", Dr. T. E. Wilson.

Sunday, September 13: 9.30 a.m., "Rheumatic Fever and Acute Rheumatism", Dr. S. E. L. Stening; 11 a.m., "Resuscitation", Dr. Gwen Bernard; 2.30 p.m., "Surgery of the Hand", Dr. T. E. Wilson; 4 p.m., "Pædiatric Problems in General Practice", Dr. S. E. L. Stening.

The fee for the course will be £3 3s. Those wishing to attend are requested to notify Dr. H. M. Webber, Honorary Secretary, Border Medical Association, 543 Kiewa Street, Albury.

Corrigendum.

IN the issue of August 8, 1953, on page 227, at the foot of the first column, Dr. Bryan Dowd, of Sydney, is reported as having stated that he did not agree that they should all learn to speak the new language of milliequivalents. This was incorrect. Dr. Dowd stated that he did agree. We regret the error.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1950, as duly qualified medical practitioners: Allen, Joseph Arthur Lancelot, M.B., B.S., 1953 (Univ. Sydney); Atkins, Christine Isobel Meredith, M.B., B.S., 1953 (Univ. Sydney); Clarke, June Rosemary, M.B., B.S., 1953 (Univ. Sydney); Dains, Mary Patricia, M.B., B.S., 1953 (Univ. Sydney); Downey, Dorothy Celia, M.B., B.S., 1953 (Univ. Sydney); Flower, Willoughby, M.B., B.S., 1953 (Univ. Sydney); Hammond, David Gwynne, M.B., B.S., 1953 (Univ. Sydney); Hu, Frank Tsu-Chang, M.B., B.S., 1953 (Univ. Sydney); Lubimoff, Veronica Jarmena, M.B., B.S., 1953 (Univ. Sydney); Lucas, Frank Samuel, M.B., B.S., 1953 (Univ. Sydney); McCaskill, Mairi Alice, M.B., B.S., 1953 (Univ. Sydney); McFadden, Geoffrey Murdoch, M.B., B.S., 1953 (Univ. Sydney); McGovern, Gregory Joseph, M.B., 1953 (Univ. Sydney); Mangraviti, Norman Joseph, M.B., B.S., 1953 (Univ. Sydney); Mumford, Joyce, M.B., B.S., 1953 (Univ. Sydney); Price, James Arthur Harold, M.B., B.S., 1953 (Univ. Sydney); Regan, William, M.B., B.S., 1953 (Univ. Sydney); Rew, Kenneth John, M.B., B.S., 1953 (Univ. Sydney); Roberts, Thomas Leslie, M.B., B.S., 1953 (Univ. Sydney); Roper, Walter Geoffrey, M.B., B.S., 1953 (Univ. Sydney); Sanders, Gordon Edgecombe, M.B., B.S., 1953 (Univ. Sydney); Shaw-Smith, Keith James, M.B., B.S., 1953 (Univ. Sydney); Sheahan, Denis John, M.B., B.S., 1953 (Univ. Sydney); Spence, Barry Blackwood, M.B., B.S., 1953 (Univ. Sydney); Stanbury, John Gregory, M.B., B.S., 1953 (Univ. Sydney); Summerhayes, Winston Joseph, M.B., B.S., 1953 (Univ. Sydney); Tinning, Robert Noel, M.B., B.S., 1953 (Univ. Sydney); Vidor, George Ivan, M.B., B.S., 1953 (Univ. Sydney); Voloshin, Olga, M.B., B.S., 1953 (Univ. Sydney); Warden, David Barton, M.B., B.S., 1953 (Univ. Sydney); Weinrauch, Ludovic, M.B., B.S., 1953 (Univ. Sydney); Whitling, William Dumas, M.B., B.S., 1953 (Univ. Sydney); Davenport, John, M.B., B.S., 1952 (Univ. Adelaide); Porritt, John Arnold, M.R.C.S. (England), L.R.C.P. (London), 1950; Kelly, James Hamilton, L.R.C.S., L.R.C.P. (Edinburgh), 1942, L.R.F.P.S. (Glasgow), 1942.

Diary for the Month.

SEPT. 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
SEPT. 14.—Victorian Branch, B.M.A.: Finance Subcommittee.
SEPT. 15.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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